# THE MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—23RD YEAR. SYDNEY, SATURDAY, AUGUST 8, 1936. No. 6.

## Table of Contents.





## Listerian Oration.[1]

### NON-SPECIFIC THERAPY AND THE VEGETATIVE REGULATION OF THE BODY.

By SIR C. STANTON HICKS, M.D., Ch.B., M.Sc., Ph.D., F.I.C., F.C.S.,
*Professor of Human Physiology and Pharmacology, University of Adelaide.*

IT is with some diffidence that I stand before you this evening, charged with the duty of delivering the oration with which your Branch honours the memory of Lord Lister.

In the first place, the words attributed to Mark Antony by Shakespeare are truly applicable to me—I was even unaware as to the correct definition of an oration until I searched the pages of the "Shorter Oxford Dictionary". In the second place, my choice of subject must appear to indicate a rather wide interpretation of the meaning of the occasion. I can only crave your indulgence upon the first count, whilst upon the last I can at least claim in justification that Lister was a man whose investigations show him to have been keenly interested in physiological function—to cite only his discovery that the contractile tissue of the iris is smooth muscle, and his proof that instead of coagulation of the blood being produced by the liberation of ammonia, it is due to damage of the vessel walls.

Since, however, the name of Lister will be honoured as long as men practise the art of healing, it is necessary for me only to dedicate my contribution to the occasion, and I have therefore selected

[1] Delivered at a meeting of the South Australian Branch of the British Medical Association on May 28, 1936.

an aspect of medical research to which our own school has made some small contribution and which has the appropriate merit that it opens up a new approach to therapeutics.

The discovery of infective agents and the further discovery of specific means to combat them have focussed our attention upon one aspect of disease to the exclusion of many others. Even at the time when Virchow[1] was laying the foundations of modern cellular pathology, there were not wanting many who felt that he was excluding too much. Perhaps, however, this is bound to happen in all human intellectual advance. It reflects, no doubt, the pattern of the mind itself. It was just at this period that the famous French physiologist Claude Bernard[2] drew attention to another aspect of the phenomenon of disease, and one which, moreover, was to remain uninvestigated for many years. He stressed for the first time the extreme importance of the constancy of the *milieu* for the living cells and tissues. Greisinger, on the appearance of Virchow's great work, wrote:[3]

> It appears to us that in this work the rôle of cells and cell derivatives is exaggerated at the expense of those antecedent phenomena in the blood and nerves.

It was, however, only natural that Virchow should claim attention. He offered a new basis for testing diagnosis and a new weapon for investigating disease processes in so far as they were reflected in the altered structure of the cellular tissues. It was indeed as natural that ancient non-specific methods of treatment, hydrotherapy for example, which was as old as Hippocrates, should fall into disrepute in the face of the new principle of morphological localization of the disease process. It is just this very subject of non-specific therapy which I propose to take up and illuminate with the light of the clinical and scientific research of the last decade.

The terminology is well known to you all: protein shock therapy, non-specific protein activation, fever therapy, acidosis therapy, and so on. Perhaps it was Wagner-Jauregg's malaria therapy of quaternary syphilis, which had its spectacular success where specific means had failed so signally, that focused the average medical practitioner's attention more closely on this subject. The fact is, however, that we are now more or less prepared to use non-specific methods, in so far as they have been indicated by the experience of others. I now propose to make an attempt to correlate various apparently unassociated physiological phenomena which are involved in this reaction of the organism to non-specific therapeutic methods, and to deduce therefrom the principles underlying the action of such methods as a guide to therapeutic advance.

Let us consider for a moment some of the contemporaneous events following upon an acute febrile infection of short duration (Table I).

There is ample evidence that the febrile state is associated either with over-action or increased reactivity of the sympathetic system,[4][5] it being scarcely necessary to indicate here that the raised metabolism, mobilization of blood sugar, constriction of skin vessels with consequent conservation of heat, and increased cardiac rate, all occurring in fever, are caused through the agency of the sympathetic nervous system.

TABLE I.
(See F. Hoff, *Vertrag XLV Kongress*, Wiesbaden, March 31, 1930.)

| Febrile Phase. | Recovery Phase. |
|---|---|
| Rise in body temperature. | Fall in body temperature. |
| Rise in basal metabolic rate. | Fall in basal metabolic rate. |
| Rise in blood sugar. | Fall in blood sugar. |
| Increased cardiac rate. | Recovery of cardiac rate. |
| Increased protein breakdown. | Diminution of protein breakdown. |
| Fall in blood cholesterol. | Rise in blood cholesterol. |
| Fall in alkali reserve. | Rise in alkali reserve. |
| Increase in ionized calcium. | Diminution of ionized calcium. |
| Leucocytosis with especial increase in neutrophile cells. | Fall in total number of leucocytes with relative increase in lymphocytes and eosinophile cells. |
| Sympathetic preponderance. | Parasympathetic preponderance. |
| Increased formation of granular cells. | Diminished production of granular cells. |

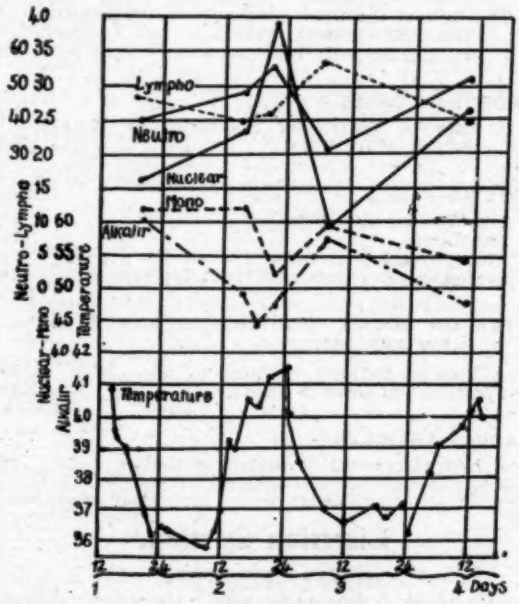


FIGURE I.
Regular alterations in temperature, acid-base equilibrium and blood picture in malaria. (After Hoff, "Non-Specific Therapy", 1930.)

Again, the fall in alkali reserve has been shown to be due to sympathetic action involving the associated increase in ionized calcium in the blood. The second phase of reaction in the opposite direction would appear to be a "biological rule of general significance", to cite the words of a prominent worker in this field (Hoff[6]). We have shown in Adelaide that this is the case with the menstrual cycle.[7] The sympatheticotonic premenstrual phase is associated with increased metabolism and sensitivity to adrenaline, whilst others have demonstrated[8][9] the associated tendency to neutrophile leucocytosis, acidosis and increased calcium ioniza-

tion in the blood. During the menstrual period itself the reverse phase sets in, whilst in parturition the same phenomena are manifest to a more pronounced degree.

If we now consider all the conditions under which we can demonstrate these same manifestations of preponderance of one or other aspect of the vegetative system, we find them to include such widely divergent states as the following: acute infectious fever; severe muscular exercise; menstrual cycle; paroxysmal hæmoglobinuria; injection of foreign protein; asthma; influence of skin stimulation, for example, hydrotherapy; injection of colloidal sulphur; hæmorrhage into the floor of the third ventricle; injection of air into the third ventricle; peroral administration of certain drugs, for example, tetrahydronaphthylamin, phenyl-ethyl-hydantoin.

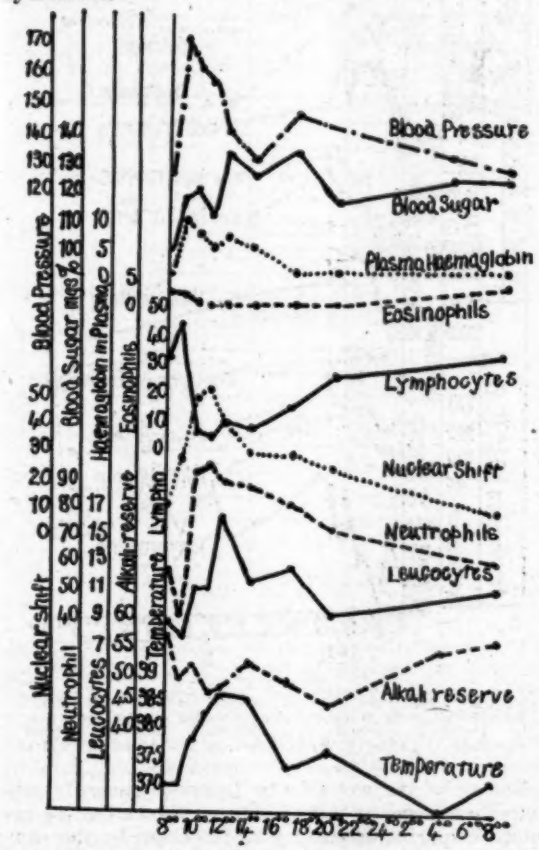


FIGURE II.

Regular alterations in blood composition, blood picture, blood pressure and body temperature in an attack of paroxysmal hæmoglobinuria. (After Hoff and Kels, from *Deutsches Archiv für klinische Medizin.*)

The simple fact that such varying causes give rise to the same complex results indicates that these are subject to a common biological coordination, and we get an insight into this mechanism in the work of Isenschmid and Krehl,[10] as well as that of Freund and Grafe.[11] These investigators, following Claude Bernard's observations,[12] have proved beyond doubt that severance of the cervical cord completely prevents the usual febrile response to injection of foreign (bacterial) protein; that is, there is no rise of temperature involving both vasomotor restriction of heat loss and increased metabolism, and no increased destruction of

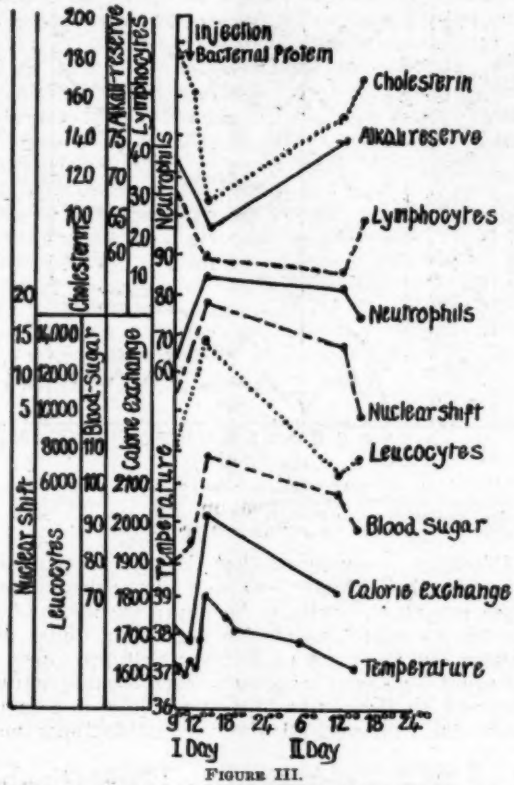


FIGURE III.

Morphological and chemical alterations resulting on injection of bacterial protein in man. (After F. Hoff, *Vortbildungs Vortrag*, 1930.)

protein. More recently, Hoff[13] has shown that the same operative procedure prevents the development of the usual morphological changes in the blood, that is, the neutrophile leucocytosis and shift of the Arneth index to the left. Grafe has extended his work to show that the general metabolism is controlled from vegetative centres in the diencephalon.

It is evident from this work that in some manner all the previously mentioned methods of "non-specific" alteration of bodily functions act in a similar way upon some part of the vegetative system, causing through its agency the coordinated changes enumerated. The conception of sympatheticotonic and parasympatheticotonic, introduced by Eppinger and Hess,[14] thus begins to assume fresh importance, and it is only necessary to remind you that W. R. Hess's[15] now epoch-making contribution to an understanding of the phenomenon of sleep proves that in the twenty-four hours' rhythm of mammalian life these two aspects of vegetative regulation show alternating preponderance, such

that sleep is conditioned by relative over-action of the parasympathetic system. Cloetta has at the same time demonstrated that during sleep the blood calcium falls, rising again in the waking stage.[16][17]

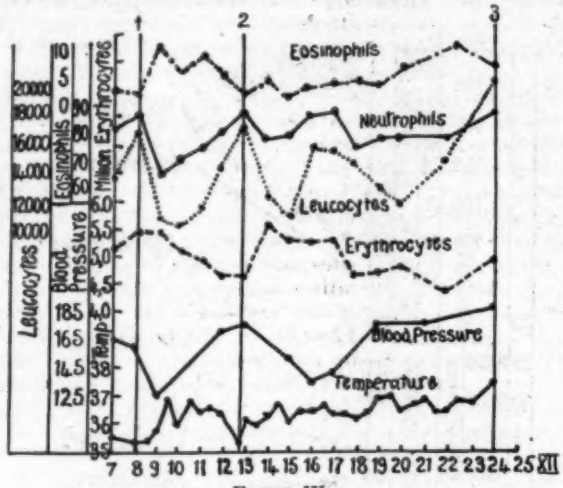


FIGURE IV.

Variations in vegetative regulation consequent upon repeated cerebral hæmorrhage. (From *Verhandlungen der deutschen Gesellschaft für innere Medizin*, XLV *Kongress*, 1933.)

It will be remembered that the strict separation of sympatheticotonic and parasympatheticotonic types proved clinically to be impracticable, and in the two phases of vegetative regulation under discussion one must not expect in all clinical cases to get equal degrees of response in each organic feature studied. In the course of a pneumonia or a septic fever, for example, all the various features may

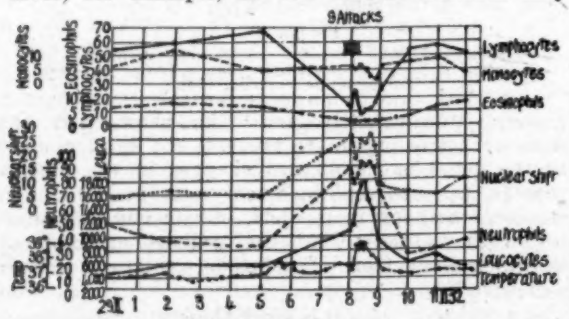


FIGURE V.

Alterations in blood picture during epileptic attacks. (After F. Hoff, *Klinische Wochenschrift*, Volume II, 1932, page 1751.)

follow the rule, whilst a leucopenia may persist, or even an agranulocytosis supervene. The temperature may drop suddenly, leaving the other features of the first phase unaltered. The same is true of variations in the response to protein shock therapy—preceding the leucocytosis there may be a sharp fall in the total count. Following an injection of bacterial protein, a rapid and extensive leucocytosis, with only slight acidosis, may be noted, whilst, on the other hand, an acidosis produced by ammonium chloride in the course of, say, nephritis therapy, is unassociated with a febrile reaction. These differences depend more often than not upon the therapeutic technique as well as upon the dosage and the interval between administrations. This aspect of the phenomena is well illustrated by a series of experiments by Hoff (see Figure VII), which makes it clear that one can at will bring about any type of febrile response and associated blood picture, ranging from high-grade leucopenia to massive leucocytosis.

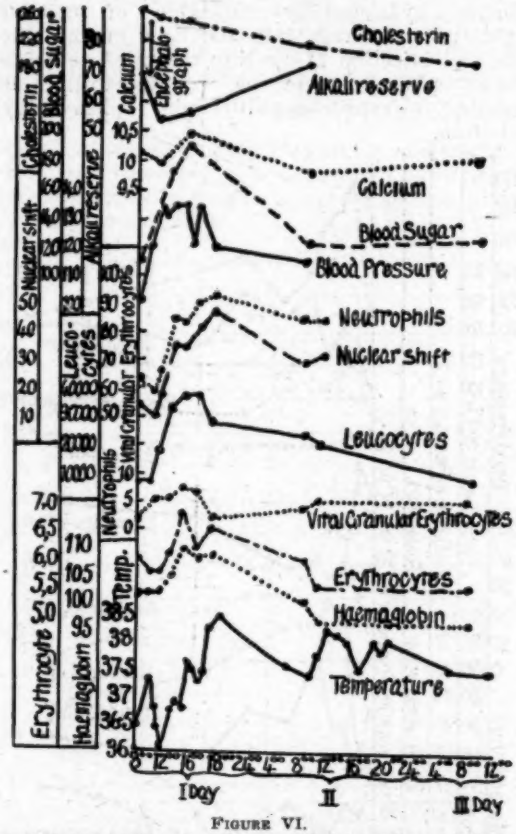


FIGURE VI.

Regular alterations in blood composition and morphology as well as body temperature following encephalography by Dandy's method (air injection into the third ventricle). (After F. Hoff, *"Vortrag"*, Wiesbaden, 1933.)

Not only are we able to increase general resistance to disease by non-specific methods, but we can enhance specific immunity to infection by the same means. This being the case, it seems reasonable to assume, at least in part, an implication of the vegetative system in antibody formation. Bogendörfer[18] has been able to prove experimentally that the agglutinin reaction to paratyphosus *B* could not be established in the blood of animals after severance of the cervical cord, owing to the cutting off of vegetative nervous impulses.

As these hitherto unassociated facts take their place in this new orientation, otherwise obscure phenomena become explicable, such as, for example,

the well-established fact that the most widely differing modes of non-specific therapy often achieve the same end result. Moreover, the essential difference between the course of a chronic and an acute infection seems to lie in the difference in vegetative response thereto. If the condition is acute, the normal response is along the lines indicated in the table and the various charts

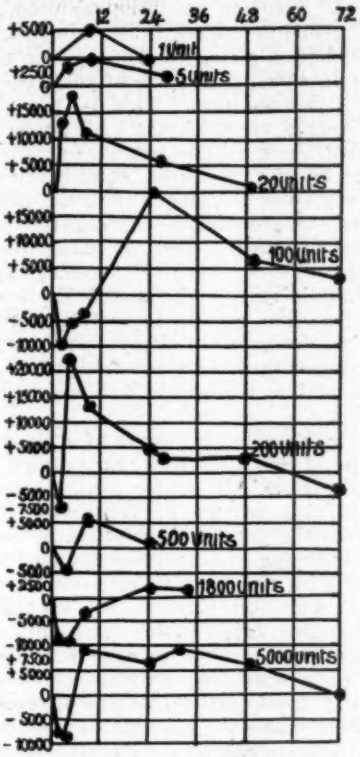


FIGURE VII.

Dependence of leucocyte response upon dosage of activating protein. (After F. Hoff, "Non-Specific Therapy", 1930.)

exhibited, whilst in chronic conditions we often find that we can with advantage provoke the "normal" response by non-specific means. This has, of course, been dramatically demonstrated in the treatment of quaternary syphilis, and every practitioner can enumerate cases of chronic disease which have improved after an acute intercurrent infection or even after a major surgical operation. The "sympathetic" reaction therefore would appear to be a physiologically protective reaction involving the whole organism.

If we now consider more closely the advances in pure physiology during the same period as that covered by this investigation of the non-specific immunity reaction, we find some outstandingly significant correlative features. We now accept it as proven that when either a sympathetic or a parasympathetic nerve is stimulated, the nervous impulse ends in the production of a chemical messenger which is the connecting link between nerve and responding tissue. In the case of the sympathetic, the humoral transmitter is an analogue of adrenaline, if not adrenaline itself, whilst in the case of the parasympathetic it is acetylcholine. This brings us into a period of "newer humoral pathology", which is part of the rapidly extending field of hormonal pathology. Without doubt this is the most important aspect of modern physiological research, and one which is likely to bring in its train even greater advances in medicine than resulted from the application of bacteriological research to the elucidation and cure of human ills.

More than ever are those words of Claude Bernard applicable to pathology: "departures from the constancy of the *milieu* are decisive causes of diseased conditions". We need cite only goitre, tetany, rickets, diabetes, sexual disorders, metabolic disturbances generally, anterior pituitary syndromes and the anæmias. It is obvious to all that every advance in knowledge of the chemistry of the vitamins opens up the possibility of new integrations in knowledge of these complex aspects of medicine.

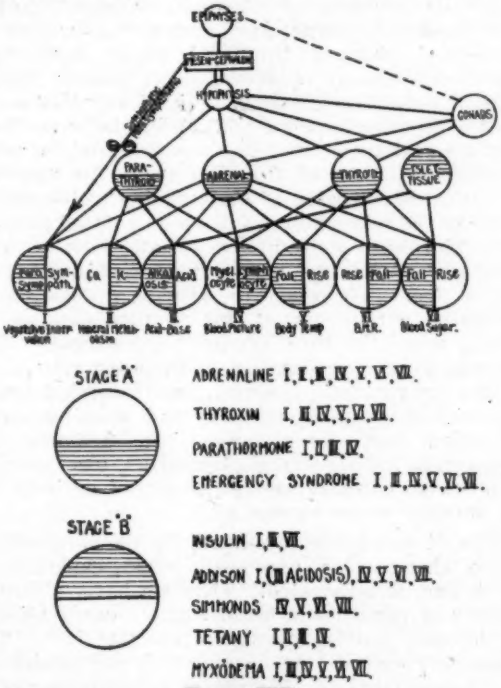


FIGURE VIII.

Schema of the vegetative regulation. (After F. Hoff, *Klinische Wochenschrift*, Volume XIV, 1934, page 519.)

In order to summarize these vegetative reactions and to indicate the interplay of the component parts of the vegetative regulating mechanism, it is perhaps better to make use of a diagram, and that of Hoff shows at a glance the main correlations. The lower circles may be taken as partially geared together, that is, they rotate in the manner anticipated from such gearing, but not necessarily to the same extent in all cases. If now we take each circle in turn and discuss the facts depicted thereby,

we find that it has been demonstrated that in fever the mineral metabolism is involved, and that there is a preponderance of ionized calcium over ionized potassium (Kraus and Zondek[19]). This same ionic balance is involved in rickets, tetany and excessive parathyreoid activity, and is better written according to György: $\frac{K.PO_4.HCO_3}{Ca.Mg.H}$. Alterations in this ionic relationship are involved in alkalosis and acidosis (Rona and Takahashi[20]), as indicated in Circle III. The next circle, Number IV, depicts the extent to which the formed blood elements are involved. We now know that in practically all instances in which the sympathetico-tonic position is adopted, the myelotic blood picture results. This has been established by Hoff for increase of calcium ions, acidosis (diabetes) and rise of body temperature.[8] In all these cases both rise of temperature and increase of metabolism are associated phenomena, which, it will be seen, must be the case if the circles rotate in unison. Circle V shows that metabolism rises in acidotic conditions and falls in states of alkalosis (Wilder, Boothby and Beeler,[21] Jalm and Sturm[22]), while the associated changes in blood sugar have been reported by many observers. The closely related central nervous connexions of V, VI and VII would lead us to expect such a relationship between them. The connexions in the diagram indicate the sense in which changes of function are to be expected within a short period of time, during which one or other of the related circles has been rotated through 90°. Thus with a rise in sympathetic activity, from whatever cause, we may expect mobilization of sugar from glycogen, to provide a source of increased energy output due to increased metabolism, which in turn produces more heat. This increased heat production is furthermore, by the same sympathetic mechanism, coupled with diminished skin circulation, and therefore heat retention and fever, whilst an acidosis and hyperpnœa are associated phenomena, together with accelerated cardiac rate, which is not entirely due to elevated temperature.

The diencephalon is essentially the mediator of these changes, as previously cited experimental work has demonstrated. Thus we have, following upon a severe drop in blood sugar concentration, a rapid mobilization of sugar from the liver. This commonly exceeds the normal with the production of a hyperglycæmia. The reverse hyperinsular effect is seen after an injection of adrenaline, which rapidly mobilizes sugar from the liver and so calls forth the opposite response. This explains the so-called biphasic action of the hormones, as well as the fact that purely sympathetic or parasympathetic preponderance is seen only for short periods. Already during the one or other phase the compensatory changes in some of the factors set in, and very soon we get a mixed picture with varying degrees of change in the different components. Thus physical exertion for a brief period leads to a clear-cut picture of sympathetic preponderance, whilst athletic training leads to the reverse phase, characterized by alkalosis and relative lymphocytosis.[23] The acute stadium of Graves's disease is associated with a similar sympathetic imbalance, but this soon passes, with the full development of thyreotoxicosis, into a complex phase in which compensatory parasympathetic factors are detectable—to cite only the lymphocytosis and alkalosis.

If the "A" position has been adopted, the compensation principle means that, before the normal is reestablished, a swing to the opposite phase will be evident in some, if not all, of the linked factors depicted in the diagram. This is, too, dependent upon the degree to which the "A" phase has been predominant, just as the extent to which a pendulum passes the point of equilibrium depends upon the degree of displacement to the one or other side. This over-correction, or "negative phase" as the clinical expression goes, is exemplified in the change from fever, cardiac acceleration, raised basal metabolic rate, and neutrophile leucocytosis, which, before the return to strictly normal conditions, is often followed by bradycardia, subnormal temperature, and lowered metabolic rate associated with a leucopenia with relative lymphocytosis.

Let us now examine the effect of a given hormone in the light of this synthesis. Suprarenal, thyreoid and parathyreoids all induce sympathetic preponderance in this scheme of vegetative regulation. Insulin from the pancreatic islet tissue antagonizes these by inducing the reverse change. Our own experience with the cortical hormone tends to support the conclusion that at all events the one termed "Cortin" favours the sympathetic orientation, whilst recent work proves that injection of "Cortin" in a sensitized animal prevents anaphylactic shock. Both adrenaline and thyroxin induce the complete chain of sequelæ enumerated under sympathetic preponderance. Parathormone, too, by acting through the calcium-potassium-phosphate balance, induces an acidosis arising from preponderance of calcium over potassium ions in the blood together with depression of $[PO]_4$ ions. It is just this change which depresses the muscle irritability in tetany and which is, of course, associated with an acidosis and disturbance of the $\frac{K.PO_4.HCO_3}{Ca.H.Mg}$ ratio. The basis of the antagonism of adrenaline, or thyroxin, and insulin can now be seen in its entirety. The islet hormone acts mainly by its control of sugar metabolism, but also through the medium of the acid-base equilibrium.

Let us now consider the actual vegetative mechanism as a whole. From the diagram it is at once seen that the hypophysis and diencephalon are placed in a key position. This conclusion is the result of rapidly accumulating evidence, which indicates that it is difficult to separate these two portions of the base of the brain, even though anatomically the hypophysis itself has only remnants of neural structure. We know that disease affecting the floor of the third ventricle can produce similar

clinical syndromes to disease of the anterior portion of the pituitary gland itself. This supports the conclusion that some of the hormones produced in this gland are elaborated by the adjacent portion of the brain. Into this category fall such conditions as *diabetes insipidus* and *dystrophia adiposo-genitalis*. The hypophysis itself is now known to elaborate at least seventeen hormones. From the posterior lobe we have oxytocin and vasopressin (Kamm[24]); possibly also a fat metabolism hormone, the so-called lipoitrin of Raab.[25] There is, too, a possibility that vasopressin may contain an antidiuretic fraction. The anterior lobe is a veritable fountain of hormones, giving rise to at least thirteen, most of which have been separately identified. These are the follicle-ripening hormone (Aschheim and Zondek[26]), the luteinizing hormone (Kraul[27]), the thyreotropic (Aron, Janssen and Loeser[28][29]), and parathyreotropic hormones (Anselmino and Hoffmann[30]), the pancreatropic (Burn,[31] Olmstedt and Logan[32]), and corticotropic hormones (Selye, Collip and Thomson[33]), the growth hormone (Evans[34]), and the fat metabolism hormone (Anselmino and Hoffmann[35]), the contrainsular hormone (Houssay[36] and Lucke[37]), the lactation hormone (Corner[38]), the melanophore hormone (Hogben and Winton[39]), the pigment hormone (Zondek and Krohn[40]), from cow only, and aduiretin, an antidiuretic hormone from the intermediate lobe.[41]

When we are faced with this formidable list of adenotropic hormones, we are forced to the conclusion that the hypophysis, even if it be not the seat of the soul, is largely in control of all other glands of internal secretion. There is ample evidence that the state of balance which we may term normal, is associated with mutual influence of these glands with each other and with the hypophysis. The evidence is in some instances incorporated in experimental work of singular perfection, and it goes to explain why primary disease in one of these glands may be associated with alteration in function and structure of the hypophysis. Thus we have anterior pituitary dysfunction and cellular alteration in Addison's disease[42] and after castration.[43]

The ways in which such interaction is brought about are three in number. There is first the direct nervous connexion between the diencephalon (floor of the third ventricle) and a gland or glands of internal secretion, the second stage in the transmission being thereafter hormonal. This is seen, for example, when for any reason the floor of the third ventricle is stimulated, for instance by hæmorrhage. Secondly, we have the hormones themselves acting, such as the adenotropic hormones of the hypophysis, or altered blood composition itself acting humorally, such as by altered acid-base equilibrium. Finally, there is the direct humoral effect of changes in blood composition upon the hypophysis-diencephalon system. We see this demonstrated in a striking manner when a fall in concentration of blood sugar acts via the hypophysis, liberating adrenaline from the suprarenals, and when the blood sugar changes are paralleled by alterations in insulin output, only when the hypophysis is intact.

The biphasic nature of the vegetative response, which, as has been already stated, appears to be of the nature of a biological law, explains why we find such clinical conditions as alkalosis and lymphocytosis in the late stages of thyreotoxicosis; or a relative lymphocytosis and alkalosis in the intensively training athlete. The interrelations, depicted diagrammatically, explain also why tetany may be combated equally well by administration of calcium or parathormone or vitamin *D* (calcium mobilization) or ammonium chloride (acidosis). The fact that glycosuria may result equally from hypophyseal tumour, hypoinsular function or hyperthyreoid function is as evident from a consideration of these interrelations as is the reverse condition of hypoglycæmia in hyperinsular function, in Addison's disease with depressed suprarenal activity, and in Simmond's disease with hypopituitary activity, leading to depressed action of the suprarenal cortex. In the last-mentioned case the contrainsulin action of the anterior lobe is carried out via the sympathetic supply of the suprarenal.

Hoff has reported a case of *osteitis fibrosa generalisata* with tumour of both the parathyreoid and anterior pituitary (basophile cell),[44] whilst the peculiar hirsutism and excessive gonad activity, associated with so-called interrenal tumour, may be produced by basophile adenoma of the anterior pituitary lobe. Complex syndromes such as these stand in their proper relations when viewed in the light of a coordinated neuro-hormonal control of the vegetative system.

### Practical Deductions.

As our first practical application of the principles of vegetative regulation, let us consider an asthmatic attack with its parasympathetic criteria of lymphocytosis, eosinophilia and bronchoconstriction. We may counteract this parasympathetic muscular stimulation with the belladonna group of drugs, or with papaverin, which may be given intravenously in severe cases. On the other hand, we may initiate a reversal of the parasympathetic preponderance by administering adrenaline, ephetonin or ephedrin. Again, we may utilize the sympathetic stimulation which can be provoked by increasing the ionized calcium in the blood, through the administration of calcium chloride. This will also bring about a reduction of the alkali reserve. Both of these sympatheticotonic factors act favourably upon asthmatic cases. Calcium may be given intravenously in doses of ten cubic centimetres as 10% calcium chloride, or as "Calcium Sandoz", which can be given intramuscularly.

The dietary treatment of asthma, which is the logical extension of the foregoing, aims at decreasing the available base in the blood by utilizing acid-producing foods, such as meat, cheese, rice or oatmeal. The effect of this may be increased

by administration of ammonium chloride. Storm van Leeuwen has induced artificial fever by injecting colloidal sulphur in the successful treatment of asthma, whilst Hoff has similarly utilized bacterial protein.[45] In stubborn cases this method is conducted so as to produce febrile reactions similar to those of malaria during a period of some weeks. Another successful method of non-specific stimulation of the vegetative regulation in asthma is that of skin irradiation by a powerful source of light (Strümpell), whilst X radiation has proved effective in the same manner. The fact that the therapeutic result persists, even when the negative, parasympatheticotonic phase sets in after cessation of treatment, indicates to what extent the alteration of the vegetative regulation of the body may establish organic change.

Closely related to the asthmatic attack is the whole range of allergic phenomena. If we take only the commoner hay asthma and the serum reaction, we find the same methods available as antidotes. This is strikingly the case, for example, when calcium is injected intravenously during the development of a serum rash, which disappears rapidly, in fact almost at once. The change is correlated with the low blood calcium associated with the serum reaction, whilst the rising calcium content runs parallel with the clinical improvement. The effect that calcium has in reducing exudative outflow from vessels, may be involved at least in preventing the spread of the urticarial rash, but the rapid removal of the existing urticaria is closely connected with the alteration in the vegetative regulation towards the sympatheticotonic side. The previously cited protection of a protein-sensitized animal by "Cortin" injection is similar in its cause.

In the group of vaso-constrictor conditions, such as Raynaud's disease, erythromelalgia, migraine, acrocyanosis and Quinke's œdema, there is every indication of preponderance of the sympathetic system, and the blood picture shows the typical neutrophile leucocytosis and high Arneth index during the attacks, with complete reversal during periods of quiescence. During the attack, therefore, the best results that so far have been obtained, are produced by attempts to establish parasympathetic preponderance. Thus acetylcholine and "Padutin", both of parasympathetic significance, have found a useful therapeutic place in this troublesome field, as well also with those cases in which organic change in the vessels has already taken place, there being still a functional component which may be influenced via the vegetative regulation. I refer to *thromboangiitis obliterans*, arteriosclerosis and diabetic gangrene.

It has long been known that a protein-rich diet worsens the spastic vascular disorders, whilst an alkalotic vegetarian diet brings distinct relief. The special position of oatmeal is to be borne in mind in this connexion, since it favours an acidosis owing to disturbance of the $Ca/PO_4$ ratio. We are beginning to realize that whether ulceration is present or not, gastro-intestinal disease is largely functional. In treatment, therefore, apart from the dietary regulation, drugs such as those of the atropine group and papaverin, are extremely valuable in combating parasympathetic over-activity and resulting spasm. The newer preparation, "Papavydrin"—a mixture of "Papaverine", 0·4 gramme, and "Eumydrin", 0·0005 gramme—and "Syntropan", 0·05 gramme, are particularly useful. Conversely, in atony of the alimentary tract, from whatsoever cause, whether central nervous disturbance or post-operative, or in peritonitis, the parasympathetic stimulant acetylcholine is most useful, or, which is the same thing, "Prostigmin", which acts by preventing destruction of the locally formed acetylcholine at the terminations of the pneumogastric nerve.

Recognition of the fundamental cause of *asthma cardiale* provides another excellent example of the application of this newer knowledge of the vegetative regulation. The nocturnal paroxysms are due to the associated parasympathetic preponderance, just as other nocturnal spasms of involuntary muscle, for example, uterus, gall-bladder, ureter, and in the first case can be prevented by the administration of morphine, which, by depressing the respiratory centre, counters the lowered threshold of response associated with the alkalosis of the parasympathetic phase, leading to periodic breathing, increasing alkalosis and anoxia.

This necessarily brief reference to the practical aspect of our theme is for the purpose, not of giving special indications, but of indicating lines along which therapeutic action can be taken with proven reference to the vegetative regulation of the body. The close connexion now known to exist between the vegetative nervous system, the glands of internal secretion, and the central nervous system through the basal ganglia should enable us to advance practical therapeutics along a wide front. Moreover, the position with regard to "physiological medicine" becomes clearer and the hitherto interesting but unanalysed curiosities of medicine suddenly take upon themselves a new significance, whilst the importance of proper psychological treatment becomes obvious. Among such conditions are: the acute onset of Basedow's disease following upon shock or anxiety; "icterus developing in a subject faced with conditions involving his very existence; or an attack of *angina pectoris* consequent upon mistaken arrest for serious crime".[45]

Here it is that we must conclude our subject, which, perhaps more than any other in the encyclopædia of therapeutics, indicates to what extent psychical, neuro-chemical and physical factors must be utilized by the physician, whose own personality itself is no minor factor in the treatment of his patient and so plays its part in rational therapy. This is perhaps the most suitable moment to express my thanks to Professor Ferdinand Hoff, Chief Physician of the University Clinic in Königsberg, by whose cooperation this presentation of the subject has been made possible.

**References.**

(1) L. Virchow: *"Cellular Pathologie"*, 1858.
(2) C. Bernard: *"Leçons sur la chaleur animale"*, 1876.
(3) W. Greisinger: *"Über das Zusammenspiel der vegetativen Regulationen"*, quoted by F. Hoff, *Klinische Wochenschrift*, Volume XIII, 1934, page 519.
(4) H. H. Meyer: *"Stand der Lehre vom Sympathicus"*, *Deutsche Zeitschrift für Nervenheilkunde*, Volume XIV, 1912, page 330.
(5) R. Gottlieb: *"Calorimetrische Untersuchungen über die Wirkungsweise des Chinins und Antipyrins"*, *Archiv für Experimentelle Pathologie und Pharmakologie*, Volume XXVIII, 1891, page 167.
(6) F. Hoff: *"Das Zusammenspiel der vegetativen Regulationen"*, *Klinische Wochenschrift*, Volume XIII, 1934, page 519.
(7) R. F. Matters: "The Influence of Menstruation on Gaseous Metabolism", *Australian Journal of Experimental Biology and Medical Science*, Volume II, 1929, page 133.
(8) F. Hoff: *"Umstimmung und vegetative Regulation"*, Wiesbaden, *Fortbildungs Vortrag*, 1930, page 39.
(9) E. Kylin and B. Silfversvard: *"Blut-Kalk-Studien. I. Technik. Physiologische Blutkalkwerte"*, *Zeitschrift für die Gesammte Experimentelle Medizin*, Volume XLIII, 1924, page 47.
(10) R. Isenschmid and L. Krehl: *"Über den Einfluss des Gehirns auf die Wärmeregulation"*, *Archiv für experimentelle Pathologie und Pharmakologie*, Volume LXX, 1912, page 109.
(11) H. Freund and E. Grafe: *"Über die Beeinflussung des Gesamtstoffwechsels und des Eiweissumsatzes beim Warmblüter durch operative Eingriffe am Zentralnervensystem"*, *Pflüger's Archiv*, Volume CLXVIII, 1917, page 1.
(12) C. Bernard: *"Leçons sur la diabète"*, 1877, page 133.
(13) F. Hoff and S. von Linhardt: *"Über die zentralnervose Regulation des Blutes"*, *Zeitschrift für die gesammte experimentelle Medizin*, Volume LXIII, 1928, page 277.
(14) H. Eppinger and L. Hess: *"Vagotonie"*, 1910.
(15) W. R. Hess: *"Der Schlaf"*, *Klinische Wochenschrift*, Volume IV, 1933, page 1284; "The Autonomic Nervous System", *The Lancet*, Volume II, 1932, page 1199.
(16) M. Cloetta and H. Thomann: *"Chemisch-physikalische Untersuchungen zur Theorie der Narkose"*, *Archiv für experimentelle Pathologie und Pharmakologie*, Volume CIII, 1924, page 260.
(17) H. Fischer: *"Die Rolle des Calciums beim Zustandekommen von Narkose und Erregungszuständen am rindenlosen und am völlig dezerebrierten Tier"*, *Archiv für experimentelle Pathologie und Pharmakologie*, Volume CXXXVIII, 1928, page 169.
(18) L. Bogendörfer: *"Über den Einfluss des Zentralnervensystems auf Immunitätsvorgänge. Beziehungen des Sympathicus zum Zustandekommen der Agglutination"*, *Archiv für experimentelle Pathologie und Pharmakologie*, Volume CXXXIII, 1928, page 107.
(19) F. Kraus and S. G. Zondek: *"Über die Durchtränkungsspannung"*, *Klinische Wochenschrift*, Volume I, 1922, page 1773.
(20) P. Rona and D. Takahashi: *"Beitrag zur Frage nach dem Verhalten des Calciums im Serum"*, *Biochemische Zeitschrift*, Volume XLIX, 1913, page 370.
(21) R. M. Wilder, W. M. Boothby and C. Beeler: "Studies on the Metabolism of Diabetes", *Journal of Biological Chemistry*, Volume LI, 1922, page 311.
(22) Jalm and Sturm: Quoted by F. Hoff, *loco citato*.
(23) H. Herxheimer: *"Zur Physiologie des Trainings"*, *Zeitschrift für klinische Medizin*, Volume XCVIII, 1924, page 484.
(24) O. Kamm: "Active Principles of the Posterior Lobe of the Pituitary Gland", *Journal of the American Chemical Society*, Volume L, 1928, page 257.
(25) W. Raab: *"Die Beeinflussung der Fettstoffwechsels durch Hypophysenstoffe"*, *Klinische Wochenschrift*, Volume XIII, February 24, 1934, page 281.
(26) S. Aschheim and B. Zondek: *"Hypophysenvorderlappenhormon und Ovarialhormon im Harn von Schwangeren"*, *Klinische Wochenschrift*, Volume VI, July 9, 1927, page 1322.
(27) L. Kraul: *"Gynäkologische Diagnose und Therapie in Fällen mit beträchtlichen subjektiven Beschwerden und negativem oder unklaren Tastbefund"*, *Wiener Klinische Wochenschrift*, Volume XLV, 1932, page 363; *"Die Beeinflussung der Hypophysen vorderlappenfunktion durch hormonalen Substanzen und deren praktischen Bedeutung"*, *Archiv für Gynäkologie*, Volume CXLVIII, 1932, page 65.
(28) M. Aron: *"L'hormone préhypophysaire excito-sécrétrice de la thyroïde"*, *Revue Française d'Endocrinologie*, Volume VIII, 1930, page 472.
(29) S. Janssen and A. Loeser: *"Die perorale Wirksamkeit des Hypophysenvorderlappens"*, *Klinische Wochenschrift*, Volume X, April 4, 1931, page 649.
(30) K. J. Anselmino and F. Hoffmann: *"Nachweis der antidiuretischen Komponente des Hypophysenhinterlappenhormons und einer blutdrucksteigernden Substanz in Blute bei Nephropathie und Eklampsie der Schwangeren"*, *Klinische Wochenschrift*, Volume X, August 1, 1931, page 1438.
(31) J. H. Burn: "The Modification of the Action of Insulin by Pituitary Extract and Other Substances", *Journal of Physiology*, Volume LVII, 1923, page 318.
(32) J. M. D. Olmstedt and H. D. Logan: "The Effect of Insulin on the Central Nervous System and its Relation to the Pituitary Body", *American Journal of Physiology*, Volume LXVI, 1923, page 437.
(33) H. Selye, J. B. Collip and D. L. Thomson: "The Anterior Pituitary and Lactation", *Proceedings of the Society of Experimental Biology*, Volume XXX, 1933, page 588; "Adrenotropic Hormone of Anterior Pituitary Gland", *The Lancet*, Volume II, 1933, page 347.
(34) E. Evans: "Initiation of Copious Milk Secretions in Virgin Goats by Anterior Pituitary", *Proceedings of the Society of Experimental Biology*, Volume XXX, 1933, page 1372.
(35) K. J. Anselmino and F. Hoffmann: *"Abgrenzung des Fettstoffwechselhormons des Hypophysenvorderlappens vom thyreotropen Hormon"*, *Archiv für experimentelle Pathologie und Pharmakologie*, Volume CLXXV, 1934, page 335; *"Über einen hypophysen Regulations-mechanismus im Kohlehydratestoffwechsel und seine Störung beim Diabetes Mellitus"*, *Klinische Wochenschrift*, Volume XIII, 1934, page 1048.
(36) B. A. Houssay: *"Diabeteserregende Wirkung des Hypophysenvorderlappenextraktes"*, *Klinische Wochenschrift*, Volume XII, May 20, 1933, page 775.
(37) H. Lucke: *"Der Kohlehydratstoffwechsel bei Erkrankungen des Hypophysenvorderlappens"*, *Zeitschrift für klinische Medizin*, Volume CXXII, 1932, page 23.
(38) G. W. Corner: "The Hormonal Control of Lactation", *American Journal of Physiology*, Volume XCV, 1930, page 43.
(39) L. T. Hogben and F. R. Winton: "Studies on the Pituitary. I", *Biochemical Journal*, Volume XVI, 1922, page 619.
(40) B. Zondek and H. Krohn: *"Hormon des Zwischenlappens der Hypophyse (Intermedin) die Rotfärbung der Erlitze als Testobjekt"*, *Klinische Wochenschrift*, Volume XI, 1932, page 405.
(41) G. Böttger: *"Pigmenthormon und Antidiuretisches Prinzip der Hypophyse"*, *Klinische Wochenschrift*, Volume XV, 1936, page 73.
(42) E. J. Kraus: *"Zur Pathologie der basophilen Zellen der Hypophyse"*, *Virchow's Archiv für Pathologische Anatomie und Physiologie und für Klinische Medicin*, Volume CCXLVII, 1923, page 421.
(43) W. Hohlweg: *"Veränderung des Hypophysenvorderlappens und des Ovariums nach Behandlung mit grössen Dosen von Follikelhormone"*, *Klinische Wochenschrift*, Volume XIII, 1934, page 92.
(44) F. Hoff: *"Richtlinien für die Behandlung vegetativer Störungen in der Praxis, Therapie der Gegenwart*, Volume LXXIX, February, 1935, page 49.
(45) S. van Leeuwen: Quoted by Hoff, *loco citato*.(44)


## BINASAL HEMIANOPIA, WITH A REPORT OF THREE CASES.


By LAURENCE DUNCAN,
*Assistant Surgeon, Victorian Eye and Ear Hospital, Melbourne.*


HEMIANOPIA implies absence of half of the field of vision of each eye; in binasal hemianopia the nasal field of vision in each eye is blind. Contrasted with bitemporal hemianopia, visual fields of such a kind as to merit the term binasal hemianopia are very rare, and when they do occur the line of demarcation is seldom one of perfect bilateral division.

### Frequency.

Fridenberg,(1) in 1896, reviewed thirteen recorded cases, and added one observed himself. Veasey,(2) in 1897, reviewed six cases recorded subsequent to the appearance of Fridenberg's paper, and added one of his own. Shoemaker,(3) in 1905, collected nineteen recorded cases and described one observed himself. Cushing and Walker,(4) in 1912, found that in a series of three hundred cases with intracranial growths, seventeen showed a tendency to binasal hemianopia, consequent in all cases upon advanced secondary atrophy.

Excluding Cushing and Walker's series associated with cerebral tumour, Table I is a brief summary of most of the recorded cases.

To recapitulate, we find that ten cases accompanied bilateral optic atrophy and three the late stages of papillœdema; two were associated with syphilitic disease about the chiasma; two were ascribed to the pressure of sclerosed carotid arteries on the lateral aspects of the chiasma or optic nerves, one to hysteria and three to a central origin. In at

TABLE I.[1]

*Reported Cases of Binasal Hemianopic Defects in the Visual Fields.*

| | Associated with or Attributed to. | Author. | Year of Publication. | Reference. |
|---|---|---|---|---|
| Optic Atrophy | Optic atrophy of *tabes dorsalis*. | W. Lang and C. E. Beevor. | 1894 | *Transactions of the Ophthalmological Society of the United Kingdom*, 1894, page 246. |
| | Optic atrophy of *tabes dorsalis*. | C. R. Heed and G. E. Price. | 1914 | *The Journal of the American Medical Association*, March 7, 1914, page 771. |
| | Optic atrophy of *tabes dorsalis*. | W. R. Gowers. | | "A Manual of Diseases of the Nervous System", Volume II, page 149. |
| | Optic atrophy of unknown origin. | Rakowicz. | 1895 | *Klinische Monatsblätter für Augenheilkunde*, 1895. |
| | Optic atrophy. | Bull. | 1895 | *Perimetrie*, 1895, page 191. |
| | Optic atrophy (Leber's familial). | Cushing and Walker. | 1912 | *Archives of Ophthalmology*, November, 1912, page 585. |
| | Optic atrophy. Six members of the same family were similarly affected, the condition considered an abiotrophy. | Daae. | 1869 | *Norsk Magasin for Lægevidenskapen*, Volume XXII, 1869. |
| | Optic atrophy following cerebral traumatism. | P. Fridenberg. | 1896 | *New York Eye and Ear Infirmary Reports*, 1896, Volume IV, page 1. |
| | Optic atrophy following a fall on the head. | Burnett. | 1900 | *Archives of Ophthalmology*, 1900, Volume XXIV, Number 1. |
| Papilloedema. | Papilloedema and developing secondary atrophy (cerebral tumour). | Eskridge | | "International Clinics", Volume I, Sixth Series, page 176. |
| | Papilloedema (cerebral tumour). | Schmidt and Wegner. | | *Archiv für Ophthalmologie*, Volume XV. |
| | Papilloedema (cerebral tumour). | C. Veasey. | 1897 | *Ophthalmic Record*, 1897, Volume VI, page 78. |
| Syphilis. | Syphilis. Gummatous exudate surrounding the chiasma. | Henschen. | 1890 | |
| | Syphilis. Gumma extending from base of brain to optic foramina. | von Graefe. | | |
| Pressure of sclerosed carotid vessels. | Pressure on the sides of the chiasma by sclerosed carotid vessels. | Herman Knapp. | 1873 | Defects in the field of vision and their connection with diseases of the heart and brain. *Archives of Scientific and Practical Medicine and Surgery*, 1873, page 293. |
| | Primary optic atrophy, with low grade of choked disc in other eye associated with arterio-sclerosis. | Cushing and Walker. | 1912 | *Archives of Ophthalmology*, November, 1912, page 588 |
| Believed to be of central origin. | Considered as one of the bizarre effects of central lesion. | von Graefe. | 1858 | *Archiv für Ophthalmologie*, 1858, Volume XI, page 258. |
| | Bilateral optic atrophy. Author believed patient had two symmetrical haemorrhages in the occipital lobes. | Herschel. | 1883 | *Deutsche Medizinische Wochenschrift*, 1883, Volume IX, page 232. |
| | Considered his case due to thrombi in both occipital lobes following cardio-renal disease. | Coppez. | 1911 | *Journal Médical de Bruxelles*, November, 1911. |
| Hysteria. | Hysteria. | Mooren. | 1867 | "*Ophthalmometrische Beobachtungen*", 1867. |

[1] In tabulating the cases, the reports of those recorded in foreign journals have been extracted from the reviews of Fridenberg, Veasey, Shoemaker, Cushing and Walker.

least thirteen of these twenty-one cases the lesion was located in the optic nerves.

Analysing the records of a consecutive series of three hundred patients with intracranial tumours, Cushing and Walker found that seventeen, or 5% to 6%, showed hemianopic defects with a tendency towards binasal blindness, consequent in all cases upon an advanced secondary optic atrophy. Concerning the previously recorded cases, they say that in fully 50% an advanced stage of papilloedema, often in association with definite brain tumour syndrome, has been shown to be the forerunner of the binasal blindness.

### Summary of Ætiological Factors.

From a consideration of the above data, let us summarize the ætiological factors in the causation of binasal hemianopia:

1. It undoubtedly occurs most frequently as a late sequel of advanced papilloedema associated with increased intracranial tension. Cushing and Walker believe that an internal hydrocephalus with distension of the third ventricle forces the optic nerves or tracts adjoining the chiasma (not necessarily the chiasma itself) downward and outward against the resistant carotid arteries.

In this way the uncrossed fasciculi to the temporal retinæ and laterally placed macular bundle as well, suffer from a mechanical pressure block in addition to the diffuse anatomical destruction of fibres throughout the nerve in consequence of the contraction of the new tissue formation in the long standing choked disc.

2. Optic atrophy may be a cause; and it may be considered under four headings.

(*a*) Of *tabes dorsalis*. The case reported by Lang and Beevor (1894) was that of a woman, aged thirty-three years. Her right vision was $^{6}/_{24}$, her left $^{6}/_{60}$. She had Argyll-Robertson pupils, optic atrophy of both disks and a binasal hemianopia. Heed and Price (1914) reported another. They

attributed the binasal defect in the visual fields to a selective optic atrophy affecting the intracranial portion of the optic nerves. In Gowers's case there was a complete loss of the lower nasal quadrant in one eye, extending, however, beyond the mid-line; in the other there was a well defined amblyopia of corresponding situation. Gowers wrote that an irregular nasal hemianopia must be found in tabetic optic atrophy and that the only case he had observed was of this variety. There seems to be no doubt that symmetrical contractions of the fields of vision do take place in tabes. Another exceptional type of alteration of the visual fields in tabes is bitemporal hemianopia. Fuchs[5] has observed a case and writes: "We must assume that the tabetic degeneration, as a rule seated in the optic nerves, may exceptionally locate itself further back in the chiasma."

(*b*) Optic atrophy of unknown origin. Rakowicz's patient was a woman, aged fifty years, complaining of failing vision. Examination revealed pallor of both optic papillæ and nasal field defects. Vision became reduced to ability to count fingers. Rakowicz concluded that nasal hemianopia was simply a condition or symptom of grave prognostic value occurring rarely in optic atrophy.

(*c*) Hereditary or familial optic atrophy. Cushing and Walker's patient was a man, aged thirty-six years. A brother, a sister and a nephew were similarly affected. Two ophthalmologists, including de Schweinitz, concurred in the diagnosis of Leber's hereditary optic atrophy. Daae, in 1869, reported a case in which five other members of the same family were similarly affected.

(*d*) As the result of cerebral traumatism. Fridenberg's patient was a man who, eighteen months previously, had struck his head in coming upstairs from a cellar. Ophthalmoscopic examination revealed greyish-white discoloration of both disks. His hemianopic condition did not improve. Burnett has reported a case following a fall on the head.

3. Syphilis. In Henschen's case *post mortem* examination revealed a gummatous exudate surrounding the chiasma; in von Graefe's case there was found a gumma extending from the base of the brain to the optic foramina. Cushing and Walker observe that a gummatous meningitis in the neighbourhood of the chiasma is doubtless capable of producing this as well as other bizarre forms of field defect.

4. Indenting of the lateral fibres of the chiasma by thickened carotid arteries—in cases of general arteriosclerosis. In 1873 Knapp suggested that extensively diseased internal carotid arteries or posterior communicating arteries might press on the outer aspect of the chiasma or optic nerve, and that nasal hemianopia or partial optic atrophy might be produced. Cushing and Walker record the case of a woman, aged fifty-two years, with general arteriosclerosis and primary involvement of nasal vision in each eye, presumably from pressure of sclerotic vessels.

5. Hysteria. In only one instance, the case of Mooren, has nasal hemianopia been recorded as occurring in hysteria.

In the cases attributed to central origin, a bilateral lesion in the occipital lobes, the hypothesis seems too conjectural, and was not submitted to *post mortem* verification.

### Case I.

Case I was one of *glioblastoma multiforme* of the right cerebral hemisphere. Double papillœdema was present, passing on to atrophy with binasal hemianopia.

On May 30, 1934, E.O'M., aged fourteen years, complained of general symptoms suggesting right frontal lobe tumour and increased intracranial pressure. The cerebrospinal pressure with a manometer attached to a lumbar puncture needle was 400 millimetres (*plus*). The vision in the right eye was $^{6}/_{36}$; in the left eye vision was $^{6}/_{24}$. Bilateral papillœdema with about four diopters of swelling was present. Examination of the visual fields revealed a binasal hemianopic defect.

Figures I, II, III and IV are copies of the fields, showing the gradual progression of the hemianopia. An unsuccessful attempt was made to remove the tumour, and on August 30, 1934, the patient died.

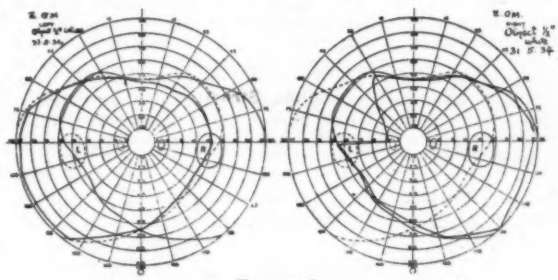

FIGURE I.
Case I. Visual fields on May 31, 1934.

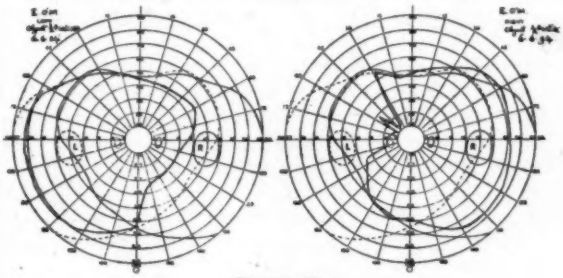

FIGURE II.
Case I. Visual fields on June 6, 1934.

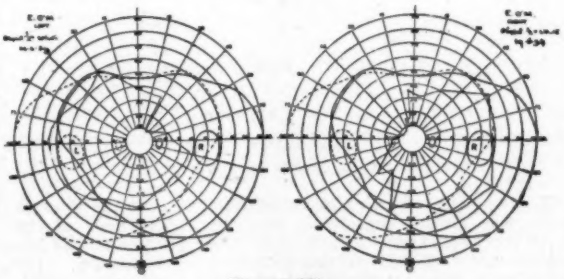

FIGURE III.
Case I. Visual fields on June 19, 1934.

*Post mortem* examination revealed in the right cerebral hemisphere a tumour weighing 84·9 grammes (three ounces) and 7·5 by 5·0 by 5·0 centimetres (three by two by two inches) in size. The diagnosis was *glioblastoma multiforme* and internal hydrocephalus.

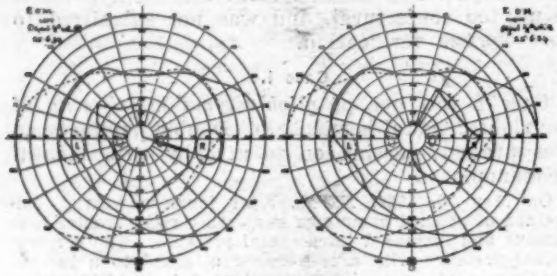

Figure IV.
Case I. Visual fields on June 25, 1934.

### Case II.

Case II was one of meningioma of the left frontal lobe. Double papillœdema was passing on to atrophy, with a binasal hemianopia defect.

On May 16, 1934, C.R., aged thirty-four years, gave a history of headaches, vomiting and failing vision. Ocular examination showed that right vision was restricted to the perception of hand movements; left vision was $^{6}/_{36}$. Double papillœdema, with about three diopters of swelling, was present. Examination of the visual fields revealed a binasal hemianopic defect (see Figures V and VI). The cerebro-spinal fluid pressure with a manometer was 400 millimetres (*plus*).

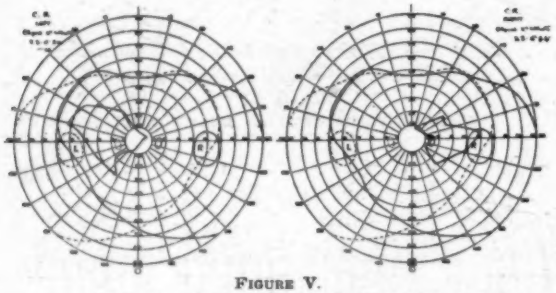

Figure V.
Case II. Visual fields on May 23, 1934.

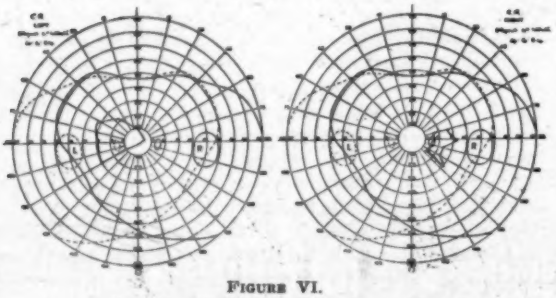

Figure VI.
Case II. Visual fields on June 4, 1934.

X ray examination of the skull showed that the *dorsum sellæ* was almost completely absorbed. The floor of the sella was somewhat uneven. The inner surface of the left frontal bone showed partial erosion and absorption. The swelling of the optic disks subsided, and a secondary optic atrophy ensued.

On December 10, 1934, Mr. Trumble performed a left frontal craniectomy, and removed the tumour. The tumour was a meningioma.

### Case III.

Case III was one of congenital syphilis; optic atrophy with a binasal hemianopic defect was present.

On October 26, 1934, J.F., aged fifteen years, gave a history of failing vision. With the right eye he could count fingers at one metre. The vision of the left eye was similar. Bilateral optic atrophy was present. Examination of the visual fields revealed a binasal hemianopic defect (see Figures VII and VIII). The Wassermann test gave a strongly positive reaction.

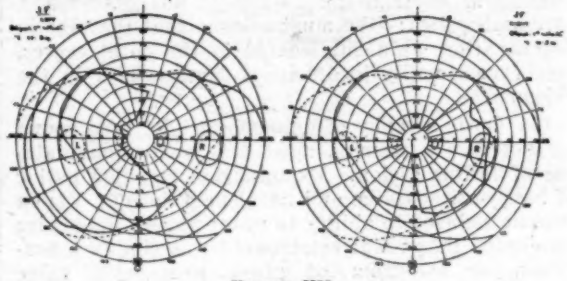

Figure VII.
Case III. Visual fields on November 7, 1934.

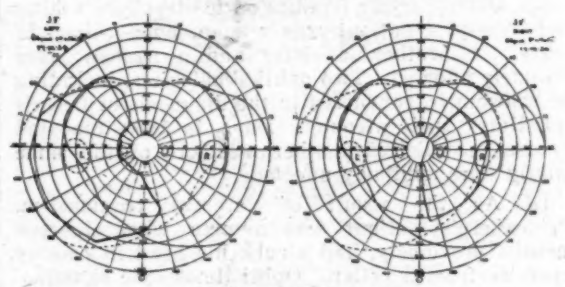

Figure VIII.
Case III. Visual fields on December 17, 1934.

The lad was placed on antisyphilitic treatment, but after a few weeks he disappeared, and did not return for observation until a year later, when his vision was reduced to ability to count fingers in only a small area in the outer temporal field of the left eye. He was admitted to Mont Park Hospital for malarial therapy.

### Summary.

A review of the literature on binasal hemianopia is given, and three additional cases are recorded. Two were associated with optic atrophy secondary to papillœdema accompanying increased intracranial tension, and one was associated with syphilitic optic atrophy.

### References.

(1) P. Fridenberg: "A Case of Binasal Hemianopsia following Cranial Traumatism", *New York Eye and Ear Infirmary Reports*, Volume IV, Part I, January, 1896.
(2) Clarence A. Veasey: "Binasal Hemianopsia, with the Report of an Additional Case", *The Ophthalmic Record*, Volume VI, 1897, page 78.
(3) William T. Shoemaker: "Binasal Hemianopsia: A Case of Neuritic Optic Atrophy with Binasal Hemianopic Fields", *New York Medical Journal*, February 4, 1905, page 215.
(4) Harvey Cushing and Clifford B. Walker: "Binasal Hemianopsia", *Archives of Ophthalmology*, Volume XLI, November, 1912, page 559.
(5) E. Fuchs: "The Field of Vision in Tabetic Atrophy of the Optic Disc", *Archives of Ophthalmology*, September, 1911, page 469.

# THE ROLE OF THE OPHTHALMOLOGIST IN THE LOCALIZATION OF CERBRAL TUMOURS.

By J. BRUCE HAMILTON, M.B. (Sydney), D.O. (Oxon), D.O.M.S. (London), F.R.A.C.S.,
*Honorary Ophthalmic Surgeon, Hobart Public Hospital; Honorary Ophthalmic Surgeon, Queen Alexandra Hospital; Honorary Ophthalmic Surgeon, Tasmanian Institution for the Blind.*

THE importance of the classical triad of headache, vomiting and optic neuritis in the diagnosis of brain tumour, as enunciated by the physicians early in the present century, has passed. The credit for this is due to the neuro-surgeons, and especially to Horsley in England, and Cushing and Dandy in America, who hastened its passing and brought to light an earlier but more complex symptomatology of these lesions. But although such credit is due to the neuro-surgeons, they have been greatly helped in the diagnosis and localization of cerebral tumour by the ancillary branches of medicine; and it is of the present part played by ophthalmologists in this direction that I wish to deal.

Sachs, in his recent work "The Diagnosis and Treatment of Brain Tumours", makes three statements of outstanding importance:

1. That the brain is the fourth most common site of tumours within the body. Sachs designates the frequency of tumours within the body in the following order: uterus, stomach, breast and brain. All medical men are conversant with the frequency of abdominal and breast tumours, but it is certain that many are not aware that the brain comes next in the list. This is due to some extent to the fact that the diagnosis of brain tumours is being relegated almost entirely to the neurologist, and consequently the possibility of their presence is overlooked by the general practitioner. But present-day medical students are tutored in the recent methods of localization and diagnosis; and the frequency of the occurrence of brain tumours is being brought directly to their notice.

2. That papillœdema, which has been a classical feature for many years, is the most important clinical sign of brain tumour. But papillœdema, on the whole, is a late—may we say a very late—symptom of increased intracranial pressure secondary to a cerebral tumour.

3. That perimetric fields are of the greatest importance in diagnosis and localization. This fact, I feel certain, is not recognized by every ophthalmologist, even if it is recognized by every neurologist. I had referred to me three years ago a patient with a suspected cerebral tumour. When I saw him he had four diopters of papillœdema and a complete homonymous hemianopia. Some four weeks before, he had consulted another oculist who found both optic discs normal, but did not determine his perimetric fields, which undoubtedly would have shown a definite defect at that stage.

### Methods of Examination.

Every patient with suspected brain tumour should undergo four essential and at least two occasional examinations. The four essential examinations are as follow:

1. Complete general and neurological examination.
2. Complete ophthalmological examination: (i) fundus examination; (ii) field examination, (*a*) with perimeter, (*b*) with Bjerrum screen; (iii) refraction and absolute visual acuity; (iv) muscle examination.
3. X ray examination of the skull.
4. Determination of the reaction of the blood to the Wassermann test.

The two occasional examinations are:

5. Complete otological examination.
6. Ventriculography.

So it will be seen that the ophthalmologist plays a considerable part in the examination of all suspected cases of intracranial tumour, and it is essential that his examination should be complete.

### Anatomy.

Before drawing your attention to the part every oculist should play in this examination, I should like to revise a few anatomical points.

All ophthalmologists are familiar with the path which a ray of light takes from the exterior to the retina, and the path the retinal stimulus traverses until it reaches the occipital cortex. For example, if a ray of light which comes from the left nasal field strikes the temporal half of the left retina, the stimulus will pass via the left optic nerve, chiasma, and left optic tract, left lateral geniculate body, left optic radiation to the left occipital cortex. Similarly a ray of light passing from the temporal half of the left retina will strike the nasal half of the left retina and pass by the left optic nerve and chiasma, the right optic tract, the right lateral geniculate body, the right optic radiation to the right occipital cortex. The nasal and temporal halves of the right field behave in a similar manner.

For a moment let us revise our knowledge of the intimate relations of this long visual pathway.

#### *Optic Nerve and Chiasma.*

The relations of the optic nerves, after they have passed through the optic foramina into the cranial cavity, are as follow: Above them lie the frontal lobes with their olfactory grooves, while laterally they are in contact with the internal carotid arteries. The relation of the chiasma to the pituitary body varies; in 79% of cases the pituitary lies beneath and in front of the chiasma, while in the remaining 21% the relations of the pituitary to the chiasma are very variable. A complete knowledge of these relations of the optic chiasma is essential for the interpretation of the visual field defects found in relation to sellar and suprasellar neoplasms.

*Optic Tracts.*

The remote and intimate relations of the optic tracts are numerable, and it should be remembered that after they sweep round the *basis pedunculi* they lie beneath the four basal nulcei on each side, namely: (i) the caudate, (ii) the lenticular, (iii) the amygdaloid, and (iv) the claustrum. Below the optic tracts lie the transverse fissures.

*The Lateral Geniculate Bodies.*

The pulvinar lies above, and the superior quadrigeminal bodies lie medially to the lateral geniculate bodies. It might be noted here that it was once thought that the visual fibres of the optic tracts ended not only in the lateral geniculate bodies, but also in the pulvinar and the superior quadrigeminal bodies. Recent investigations, however, have shown that lateral geniculate bodies are the only cell stations in this region; and further, recent clinical and laboratory researches by MacKenzie and by Penman have clearly shown that the projection of the retinal quadrants can be as clearly defined in the lateral geniculate bodies as they can be on the occipital cortex. These workers have also proved beyond doubt that there is no bilateral representation of the macula, either in the geniculate bodies or in the cortex, but that fibres from the temporal half of each macula remain uncrossed, while those from the nasal half of each macula cross at the chiasma.

*The Optic Radiations.*

Adolph Meyer has strikingly indicated the large sweep which the ventral fibres of the optic radiations take through the temporal lobes to the occipital cortices, and has shown what an extensive opportunity tumours and absesses in this vicinity have to involve the radiation. He has further demonstrated the relations of the radiations to the posterior horn of the lateral ventricles, from which the radiations are separated only by the tapetum of the *corpus callosum*.

*The Occipital Cortex.*

Gordon Holmes and Lister demonstrated the localization of the fields of vision on the medial surface of the occipital cortex, both above and below the calcarine fissures, and their work has been borne out by recent experiments.

**Signs and Symptoms.**

Having reviewed the relations of the separate portions of the optic pathway *seriatim*, I shall now discuss the ocular signs and symptoms of cerebral tumours, especially in regard to their localizing value.

*Ocular Muscles.*

*Sixth Nerve Palsy.*—Sixth nerve palsy is now generally known as one of the false localizing signs if unilateral, but it may be the precursor of a bilateral sixth nerve palsy which is almost pathognomonic of a pontine lesion. The frequency of unilateral sixth nerve palsy is accounted for by pressure of the stretched sixth nerve against the petrous bone as it crosses it.

*Weber's Syndrome.*—A growth involving one *basis pedunculi* and involving the third nerve at its emergence produces a palsy of the third nerve on the same side, with a paralysis of the face, leg and arm on the opposite side of the body.

*Benedict's Syndrome.*—A growth involving the *basis pedunculi* and the red nucleus will cause a third nerve palsy on the same side with weakness and tremor on the opposite side of the body.

*Millard-Gubler-Foville Syndrome.*—A growth involving the posterior portion of the pons will produce a sixth and seventh nerve palsy with hemianæsthesia and hemiplegia on the opposite side. But as explained under the heading of sixth nerve palsy, a unilateral sixth nerve palsy may also result from growths in diverse positions within the cranium.

*Nystagmus.*—Nystagmus is also a false localizing sign, as it is present not only in cerebellar tumours, but also frequently in cerebral tumours; and more especially in those of the frontal lobes. But it must be admitted that nystagmus is more regular in cerebellar, and more often irregular in frontal lobe tumour.

*The Presence or Absence of Nystagmus in Cerebellar Tumour.*—The absence of nystagmus in an obvious cerebellar tumour localizes the lesion to the vermis, as demonstrated at operation by Cushing; while the presence of nystagmus in an obvious cerebellar tumour may be helpful from the fact that the coarse quick jerk towards the point watched with the slow movement away, is more marked on looking towards the side of the lesion.

*Weakness of the Orbicularis Oculi.*—Weakness of the *orbicularis oculi* is a very important early sign of eighth nerve tumour, and is often apparent long before there is a generalized weakness of the seventh nerve. Conversely, facial paralysis without involvement of the *orbicularis oculi* localizes the lesion in or above the nucleus.

*Transient Diplopia.*—Transient diplopia seems to be a very common early symptom of lateral ventricle tumours, and is also occasionally found in third ventricle tumours.

*Bilateral Ptosis.*—Bilateral ptosis is a localizing sign of some importance, and suggests a lesion of the quadrigeminal plate involving the nuclei of the extraocular muscles.

*The Cornea.*

The sensibility of the cornea should always be tested as a routine measure in all cases of suspected cerebral tumour, for it is frequently found to be anæsthetic in eighth nerve tumours, and also in tumours of the Gasserian ganglion. This anæsthesia is due to involvement of the ophthalmic branch of the trigeminal nerve.

*The Pupils.*

Inequality of pupillary reaction is of no value from the standpoint of localization.

Loss of all pupillary reactions to light is most suggestive of midbrain or pineal tumours.

*Fundi.*

*Papillœdema.*—I have already referred to papillœdema early in this discussion, but I now wish to draw attention to several points in regard to it. (i) Its great frequency and early onset in cerebellar, ventricular and temporo-sphenoidal tumours are common knowledge, and are due to internal hydrocephalus. (ii) In tumours in other positions within the cranial cavity papillœdema is a decidedly late symptom. I recently saw a patient with progressive weakness of his right arm and leg, and with intense headache. His symptoms had commenced four months before, and on examination he had no fundus change and no field defect in either eye. It was only one month later that he developed one diopter of papillœdema, and a few scattered hæmorrhages in his left disk. Investigation of his brain revealed an inoperable glioma of the left Rolandic area. (iii) The absence of papillœdema in pituitary and suprasellar tumours is now an indisputable fact, except when such tumours block the foramen of Monroe, causing an internal hydrocephalus. Then the papillœdema is superimposed on a primary optic atrophy. Six years ago I saw a female patient with headache, loss of vision and amenorrhœa of seven years' duration. She had slight papillœdema superimposed on a primary atrophy. The day after admission to hospital she suddenly died, and a *post mortem* examination revealed a hæmorrhage into a suprasellar cyst, which had grown to quite extraordinary dimensions, and had undoubtedly blocked the foramen of Monroe. (iv) In olfactory groove tumours papillœdema occurs on the contralateral side, but on the ipsilateral side optic atrophy is usually found to be due to the fact that direct pressure on the nerve of that side prohibits œdema of that nerve head. It has also been found that in tumours of the frontal lobes papillœdema is sometimes a late sign; this is possibly due to direct pressure on both nerves, preventing swelling of the nerve heads. (v) Older members of the profession will remember the interesting controversy that raged in London in 1909 between Leslie Paton and Victor Horsley, regarding the significance of unilateral papillœdema, and how Leslie Paton showed from a survey of the fundi of Victor Horsley's own cases that a unilateral choked disk was of no localizing significance. Mohr has now confirmed Paton's findings and states that papillœdema is ipsilateral in 56% and contralateral in 44% of cases. (vi) Intermittent loss or disturbance of vision (coincident with papillœdema) and precipitated by change in body position is very significant of third ventricle tumours; but continuous loss of central vision is a very late complication of papillœdema and helps to distinguish it from papillitis. (vii) Papillœdema to five diopters may occur in both eyes in seven days, according to Traquair. (viii) Naturally, papillœdema *per se* causes no defect in the field of vision, except an enlargement of the blind spot. If the macula becomes very œdematous, then a relative central scotoma may occur.

*Optic Atrophy.*—I wish also to draw attention to several significant points concerning optic atrophy: (i) It has been realized for many years that *tabes dorsalis* is the commonest cause of optic atrophy; but only in recent years have pituitary and suprasellar tumours been found to run tabes a very close second in the production of primary optic atrophy. (ii) Since operative measures have been instituted for the removal of intrasellar and suprasellar tumours, it has been found that the primary atrophy produced by one of these tumours is at first only a physiological block and that if this block is relieved early, vision returns rapidly in most cases, often to normal. Hence the great importance of an early diagnosis of pituitary or suprasellar tumours. (iii) Under the heading of papillœdema we have referred to the unilateral atrophy in olfactory groove tumours with papillœdema on the opposite side. (iv) A dilated third ventricle may cause pressure on both optic nerves, with resulting atrophy and without the coincident papillœdema so common in hydrocephalus. (v) With regard to the fields of vision in optic atrophy: In *tabes dorsalis* a concentric constriction is commonly found, while in pituitary and suprasellar tumours many varieties of field defects are produced; these will be discussed under another heading.

*Angiomata.*—Lindau, before a combined meeting of the Neurological and Ophthalmic Sections of the Royal Society of Medicine, recently opened a very interesting discussion on the relation of extracranial and retinal angiomata to blood vessel tumours of the brain. These angiomata can be divided into two groups:

Extracranial Angiomata.—(*a*) Sturge and others have found that trigeminal port wine stain (commonly known as birthmark) is not infrequently associated with buphthalmos in the same eye and hemangioma of the cerebral cortex. These cerebral hemangiomata are often calcified and opaque to X rays, and often produce a defect in the visual field. Foster Moore and Aynsley, in 1929, reported interesting cases of this type in *The British Journal of Ophthalmology.* Parkes Weber, in a recent letter to *The British Medical Journal,* suggests that this clinical entity should be termed the Spurge-Kalischer disease, after the first men to describe clinical and *post mortem* cases respectively. Weber himself reported the first X ray finding of the cerebral lesion. (*b*) To these venous angiomata which never show papillœdema, Cushing has added his aneurysmal angiomata, with ipsilateral exophthalmos and slowly developing choked disks. This type may or may not show increased extracranial vascularity, but an audible bruit over the lesion is not uncommon.

Retinal Angiomata.—In retinal angiomata there is no facial angioma, but frequently a hæmangioma of the retina together with vascular cysts in the cerebellum, pancreas and kidneys. This type has been designated Lindau's disease, and I think it throws much light on these retinal conditions formerly named after Coates. Van der Hoeve

recently described in his Doyne Memorial Lecture the history of a family with Lindau's disease through three generations; and other authors have reported this hereditary tendency also. Before leaving this subject, let me quote Cushing's words with regard to fundus examination:

> The peripheral retina of every patient with the syndrome of a cerebellar tumour should unquestionably be scrutinized, for the presence of an angioma would serve to make possible a preoperative pathological diagnosis.

*Optic Nerves.*

Primary tumours of the optic nerves are not within the scope of this discussion. I have already discussed the findings of olfactory groove and frontal lobe tumours producing direct pressure on one or both nerves.

*Chiasma.*

The commonest lesion of the chiasma is the physiological block resulting from pressure of pituitary, suprasellar and third ventricular tumours. These, as already stated, produce primary optic atrophy and varied field defects. These field defects have been worked out in great detail by Cushing, Bailey and Traquair, and are as follow:

1. Bitemporal hemianopia, which is caused by the tumour's producing its greatest pressure on the crossed tracts, while a tumour pressing directly from behind produces a bitemporal scotoma. This is due to the fact that the macula fibres cross in the posterior angle of the chiasma.
2. Homonymous hemianopia, which is produced by the tumour's pressing one tract against one *basis pedunculi*.
3. Binasal hemianopia, which is extremely uncommon and is caused by the tumour's pressing the optic nerves or tracts against the calcified internal carotid arteries.
4. Blindness in one eye and a temporal defect in the other, which is quite a common finding and should be borne in mind in every investigation.
5. Frequently when there is an almost complete hemisection of the visual field in bitemporal hemianopia, a small part of the upper peripheral temporal field is left intact, producing the pathognomonic "temporal island".
6. A rapidly growing tumour may produce a centracaecal scotoma.
7. Cushing and Walker have watched the failure of the field of vision in these tumours from day to day and have found that the right field fails clockwise and the left field fails anticlockwise, and that they reform after operation in the reverse direction.

*Optic Tracts.*

Primary tumours of the basal nuclei (although not very common) do produce definite signs of pressure on the optic tracts. Lillie, of Rochester, United States of America, has recently reported three cases, in which he has observed the following characteristics: (i) homonymous hemianopia, (ii) bisection of the macula, (iii) incongruity of the visual fields, and (iv) occasional involvement of the opposite tract.

*The Geniculate Bodies.*

Primary tumours in the geniculate bodies are unknown, but pinealomata press on the geniculate bodies, causing homonymous hemianopia, and on the superior quadrigeminal bodies, causing a deficiency in the deviation of the eyes upwards.

*The Optic Radiations.*

The extreme sweep of the optic radiations makes it evident that the extent of the tumour must be enormous before one radiation can be involved in its whole width. Therefore one must expect to find not a complete homonymous hemianopia, but more often a quadrantic one, the quadrant involved varying with the site of the tumour. Should the tumour involve the dorsal fibres of one radiation, and thus should the angular gyrus become implicated, visual hallucinations of form and even visual word blindness will result. I recently saw a male, aged fifty years, with a glioma involving his angular gyrus, whose first symptom was definite hallucinations of form. One day early in the course of his disease he saw a gate, which was not present, and one week after he declared that the wall paper in his living room was covered with wattle birds and must have been changed in his absence. As would be expected with tumours in the optic radiations, the macula is usually spared.

*Occipital Cortex.*

Here again primary tumours are rare, but when they do occur the field defects are usually quadrantic homonymous anopia with sparing of the maculæ. Even when the defect becomes completely homonymous both maculæ are usually spared. This was accounted for by Lister and Holmes by the bilateral representation of each macula in the occipital cortices, but has recently been explained by MacKenzie as extensive representation of the macula on the occipital cortex. Also visual hallucinations of colour are common in this condition and have been very clearly shown in a case of meningioma recently demonstrated by Ringland Anderson.

**Conclusion.**

A fitting conclusion to this contribution is a reproduction of Traquair's table of field defects caused by usual lesions in the visual pathway. Much credit is due to Traquair for his life-long work on the interpretation of the pathological visual fields, and the value of his work has gained world-wide recognition.

**Summary.**

1. No investigation of a case of suspected intracranial tumour is complete without a full ophthalmological examination.
2. A full ophthalmological examination consists of fundus examination, field-taking, muscle examination and refraction.
3. Meticulous field-taking is possibly the most important aid to the localization of cerebral tumour at present known.
4. Papillœdema is the most positive single sign of intracranial pressure.

THE VISUAL PATHWAY AND INTRACRANIAL LESIONS. (After Traquair.)

| | | | | Field Defect. | Usual Lesions. |
|---|---|---|---|---|---|
| Extracranial | | | Optic nerve | Enlargement of the blind spot.<br>Concentric contraction.<br>Binasal hemianopia. | Papilloedema due to increased intracranial pressure. |
| Intracranial | | Subchiasmal | Optic nerve | Defects unilateral.<br>Central scotoma.<br>Hemianopia and quadratic defects. | Tumour or abscess of frontal lobe (Foster Kennedy syndrome).<br>Local tumour.<br>Disseminated sclerosis.<br>Trauma. |
| | Subgeniculate | Chiasmal | | Quadrantic temporal scotoma (junction scotoma). | Local tumour, or aneurysm. |
| | | | Anterior angle | Unilateral temporal hemianopia, passing into bitemporal hemianopia, or blindness of one eye, with contralateral lateral temporal hemianopia. | Disseminated sclerosis. |
| | | | Body | Bitemporal hemianopia. | Local tumour.<br>Disseminated sclerosis.<br>Syphilis. |
| | | | Posterior angle | Unilateral hemianopia passing into homonymous hemianopia. | Local tumour. |
| | | Suprachiasmal | Optic tract | Homonymous hemianopia.<br>Sparing of central area uncommon.<br>Quadrant defects common.<br>Defects frequently incongruous. | Local tumour.<br>Temporal lobe tumour or abscess. |
| | Suprageniculate | | Optic radiation | Homonymous hemianopia.<br>Sparing of central area common.<br>Upper quadrant defects rare.<br>Peripheral defects due to internal lesions.<br>Central defects due to external lesions.<br>Defects may be ill defined with sloping edges<br>All defects congruous. | Hæmorrhage (?).<br>Thrombosis.<br>Tumour or abscess.<br>Injury. |
| | | | Occipital cortex | Homonymous hemianopia.<br>Sparing of central area.<br>Upper quadrant defects rare.<br>Homonymous hemianopic scotomata.<br>Double homonymous hemianopia with retention of central field.<br>Peripheral defects due to anterior lesions.<br>Central defects due to posterior lesions.<br>Defects sharp edged and well defined.<br>All defects congruous | Thrombosis.<br>Tumour.<br>Injury. |

## Bibliography.


T. R. Aynsley: "Buphthalmos and Nævus", *The British Journal of Ophthalmology*, Volume XIII, December, 1929, page 612.

A. J. Ballantyne: "Buphthalmos with Facial Nævus and Allied Conditions", *The British Journal of Ophthalmology*, Volume XIV, October, 1930, page 481.

H. Cushing: "Chiasmal Syndrome", *Transactions of 13th International Congress of Ophthalmology*, Volume III, 1929.

H. Cushing: "Intracranial Tumours", First Edition.

H. Cushing and P. Bailey: "Tumours Arising from Blood Vessels of the Brain", 1928.

W. E. Dandy: "Benign Tumours of the Lateral Ventricles of the Brain", First Edition.

W. E. Dandy: "Benign Tumours of the Third Ventricle of the Brain", 1933.

H. R. Dew: "The Simulation of Pituitary Diseases by Intracranial Lesions", THE MEDICAL JOURNAL OF AUSTRALIA, December 24, 1932, page 771.

R. F. Moore: "Medical Ophthalmology", 1925.

R. F. Moore: "Hæmangioma of the Meninges Involving Visual Cortex", *The British Journal of Ophthalmology*, Volume XIII, May, 1929, page 252.

H. G. A. Gjessing: "The Importance of Eye Symptoms in the Diagnosis and Localization of Brain Tumours", *The Transactions of the Ophthalmological Society of the United Kingdom*, Volume LIV, 1934, page 581.

G. Holmes: "Suprasellar Tumours", *Transactions of the 13th International Congress of Ophthalmology*, Volume III, 1929.

W. I. Lillie: "Ocular Phenomena Produced by Temporal Lobe Tumors", *The Journal of the American Medical Association*, November, 1925, page 1465.

W. I. Lillie: "Homonymous Hemianopia. Primary Sign of Tumors Involving the Lateral Part of the Transverse Fissure", *American Journal of Ophthalmology*, Volume XIII, January, 1930, page 13.

W. D. Sheldon and W. I. Lillie: "Importance of Visual Fields in the Localization of Brain Tumors", *The Journal of the American Medical Association*, March 8, 1930, page 677.

A. Lindau: Discussion on vascular tumours of the brain and spinal cord, *Proceedings of the Royal Society of Medicine*, Volume XXIV, November, 1930, page 362.

I. Mackenzie, S. Meighan and E. N. Pollock: "On Projection of Retinal Quadrants on Lateral Geniculate Bodies and Relationship of Quadrants to Optic Radiations", *Transactions of the Ophthalmological Society of the United Kingdom*, Volume LIII, 1933, page 142.

K. B. Noad: "Simulation of Vascular Disease of the Geniculo-Calcarine Pathway by Cerebral Tumour", THE MEDICAL JOURNAL OF AUSTRALIA, September 23, 1933, page 400.

L. Paton, P. Sargeant and H. M. Traquair: "Symposium on Diagnosis of Intracranial New-Growths", *Transactions of the Ophthalmological Society of the United Kingdom*, Volume LI, 1931, page 364.

G. G. Penman: "Representation of the Areas of the Retina in the Lateral Geniculate Body", *Transactions of the Ophthalmological Society of the United Kingdom*, Volume LIV, 1934, page 232.

E. Sachs: "Diagnosis and Treatment of Brain Tumors", 1931.

M. Schmidt: "Intracranial Aneurysms", *Brain*, Volume LIII, Part IV, January, 1931, page 489.

F. A. R. Stammers: "Mutual Problems of Neurological Surgery and Ophthalmology", *Transactions of the Ophthalmological Society of the United Kingdom*, Volume LI, 1931, page 544.

H. L. Tidy: "Synopsis of Medicine", 1934, pages 956, 993.

H. M. Traquair: "An Introduction to Clinical Perimetry", 1927.

H. M. Traquair: "Fields of Vision in Intracranial Lesions", *The British Medical Journal*, August 5, 1933, page 229.

J. Van der Hoeve: Doyne Memorial Lecture, "Eye Symptoms in Phakomatoses", *Transactions of the Ophthalmological Society of the United Kingdom*, Volume LII, 1932, page 380.

F. P. Weber: "The Sturge-Kalischer Disease and the Sturge-Weber Panathenaic Amphora at Toronto", *The British Medical Journal*, April 4, 1936, page 708.


# Reports of Cases.

## A CASE OF VENTRICULAR STANDSTILL.


By WILFRED EVANS, M.B. (Sydney), M.R.C.P. (London),

*Honorary Assistant Physician, Sydney Hospital.*


THIS case is interesting because periods of cardiac asystole were observed for two days before death and an electrocardiogram was obtained during an attack.

### Clinical History.

A.B., aged fifty-four years, first came to my out-patient department at the Sydney Hospital in 1932. At that time he was under treatment for syphilis and had clinical signs of aortic regurgitation. The Wassermann test gave a completely positive reaction, and in 1933 the *T* waves were inverted in all leads of the electrocardiogram (Figure I).

In 1935 he had a severe hæmatemesis, and in January, 1936, was admitted to the Sydney Hospital suffering from congestive cardiac failure. The electrocardiogram had changed since 1933 and showed evidence of progressive

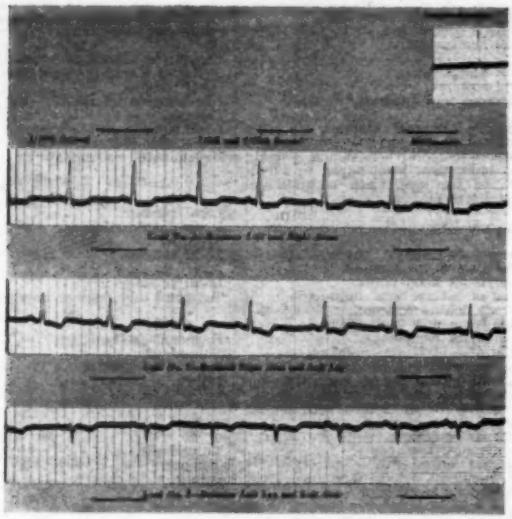

FIGURE I.
A.R., May 17, 1933.

myocardial degeneration. In Figure II it is seen that most of the cardiac contractions take their origin from the auriculo-ventricular node, but occasionally one rises from the sinus. While in hospital he complained of attacks of severe substernal pain.

Two days before death he suddenly became unconscious, his colour was ashen, the pulse and respirations ceased,

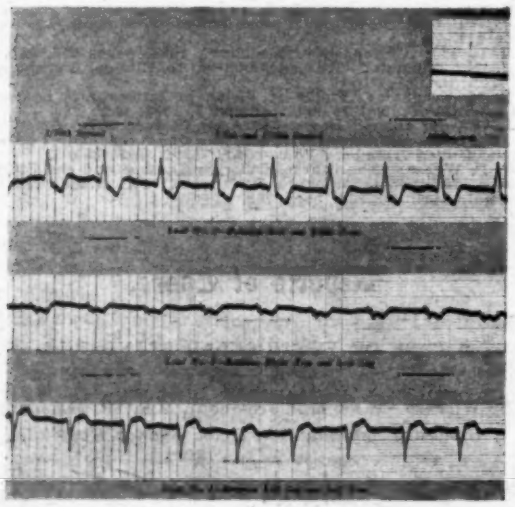

FIGURE II.
A.R., February 4, 1936.

and no heart sounds could be heard. After fifteen seconds he twitched convulsively and his pulse and colour returned. These attacks became longer and more frequent until death supervened.

The electrocardiogram showed nodal rhythm and intervals of complete ventricular standstill (Figure III).

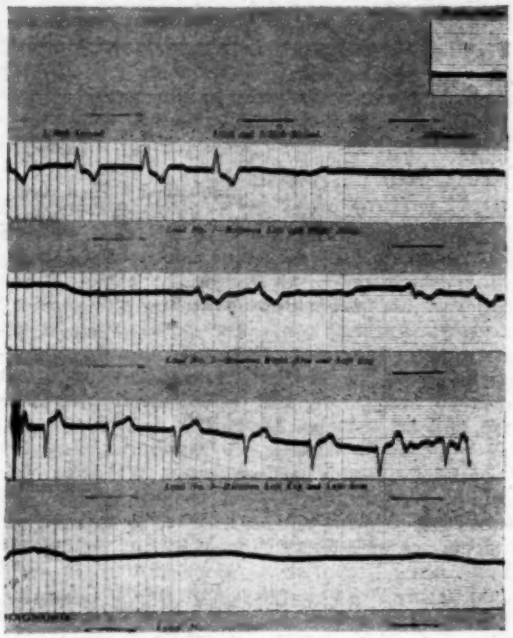

FIGURE III.
A.R., March 24, 1936. Cardiac asystole. Lead III in this tracing is continued into the space usually occupied by Lead IV, in order to show a long period of cardiac asystole.

FIGURE IV.
A.R., April 1, 1936. The heart showing syphilitic aortitis.

### Post Mortem Findings.

On *post mortem* examination gross syphilitic aortitis, involving the mouths of the coronary arteries, was found. The aortic valves were hard and calcified. The liver was greatly enlarged and its surface was coarsely granular.

Microscopic examination revealed myocardial fibrosis, chiefly affecting the left ventricle, and cirrhosis of the liver.

FIGURE V.
A.R., April 1, 1936. The liver showing syphilitic cirrhosis.

### Comment.

The cause of ventricular standstill has been attributed by some observers to vagal inhibition, but experimentally in complete heart block (the most common cause) no influence of the vagus on the ventricular rate has been demonstrated.

In the case described the periods of ventricular standstill were associated with nodal rhythm and preceded by anginal pain. They were probably caused by a diminution in the vascular supply and an abnormal situation of the pacemaker.

## Reviews.

### THE WEATHER AND DISEASE.

THE author of the first of a series of monographs on "The Patient and the Weather"[1] protests against the interpretation of disease processes only from the facts revealed by *post mortem* examination and by the technique of the laboratory. He rightly insists that the patient must be considered as a living dynamic unit in relation to his environment. He reminds us that the importance of meteorological conditions in health and disease was stressed by Hippocrates, whose name he translates humorously into modern speech as "Broncho-buster". He demonstrates that storm tracks run from west to east principally across the northern portion of the United States of America. The passage of each cyclonic storm is accompanied by barometric, thermal and humid disturbances. These demand a series of autonomic and metabolic readjustments in the human body. Certain diseases, therefore, should be characteristic of the storm zones, other diseases of the quieter areas. The relative incidence of different pathological conditions in the various States of America is shown graphically in a series of maps. The statistical material is drawn from the reports of the draft examination during the War and from the mortality tables of Canada and the United States for the years 1920 to 1930.

The author has attempted to prove from these data that meteorological conditions play the dominant rôle in determining the relative prevalence of different diseases in the United States, and has elaborated a theory of the nature of the physiological and pathological processes which lead up to these diseases. The assumptions which are employed in building up his theory do not inspire credence. The statistical facts at times are opposed to his theoretical expectations, notably in regard to obesity and tuberculosis. A sociological factor is admitted to explain unconformable figures from California, and a racial factor is suggested in regard to Quebec in similar circumstances. Elsewhere these influences are ignored.

Graphs are reproduced which indicate that children conceived in the spring are relatively liable to be malformed, mentally superior, schizophrenic or tuberculous, while children conceived in the autumn are relatively liable to be mentally deficient or to suffer from manic-depressive psychosis. These graphs are considered to be evidence of the immediate effect of climatic conditions on the germinal cells.

The statistical material which is presented furnishes numerous interesting facts. For example, people live longer in the northern than in the southern States. Syphilis is most prevalent in the subtropical south-eastern States, but tabes and *dementia paralytica* are relatively rare in these areas. Cancer is relatively common in the northern States, tuberculosis in the southern States. Skin cancer is most prevalent in the hot south-eastern States. The American negro is in general most healthy in the States of Alabama, Georgia and South Carolina. Going northerly, he is increasingly liable to congenital malformations, suicide, diabetes, exophthalmic goitre, *angina pectoris*, epilepsy, cancer, tuberculosis, erysipelas and scarlet fever. Eclampsia and furunculosis are more prevalent in the negroes of the more southern States. The negro is apparently more subject to epilepsy than the white American, and the incidence of epilepsy amongst the whites also is heaviest in the south-eastern States, where the negro population is chiefly domiciled.

[1] "The Patient and the Weather", by W. F. Petersen, M.D.; Volume I, Part 1: The Footprint of Asclepius; 1935. Ann Arbor: Edwards Brothers. Demy 4to, pp. 127, with illustrations. Price: $3.75 net.

### ANÆSTHESIA.

"PRACTICAL POINTS IN ANÆSTHESIA", by H. K. Ashworth, is intended for the student and general practitioner.[1] It is therefore simple, dogmatic and brief. Indeed, it is almost too brief. A more detailed chapter upon nitrous oxide anæsthesia, for instance, would have been more valuable to the house anæsthetist facing his first administration of this gas. Dr. Ashworth has many good things to tell, and his book would have been better had he allowed himself more room for detail.

Ether and chloroform receive, appropriately, the fullest consideration. Spinal anæsthesia (with "Stovaine") is described clearly and with a discerning note of caution. The relevant facts of basal narcosis are stated clearly and concisely, whilst regional and local anæsthesia (in

[1] "Practical Points in Anæsthesia: A Clinical Handbook for Students and General Practitioners", by H. K. Ashworth, M.B., Ch.B., M.R.C.S., L.R.C.P., D.A.; with a chapter on Local Anæsthesia by H. T. Simmons, B.Sc., M.B., Ch.M., F.R.C.S.; 1936. London: J. and A. Churchill Limited. Crown 8vo, pp. 168, with illustrations. Price: 7s. 6d. net.

so far as they concern the student or house surgeon) are well described. The practical little chapter upon respiratory and circulatory failure may be commended to all students.

The author, in tabulating the signs of ether anæsthesia, suggests that certain upper abdominal manipulations be carried out at a depth of anæsthesia at which the respiration becomes shallow and "sighing". Students tend to overdose their patients, and teaching should direct them towards the minimum depth of anæsthesia which will satisfy the surgeon's requirements rather than encourage them to enter dangerous ground. The author, too, favours the chloroform-ether sequence (Sankey's technique) in induction. In view of the treachery of chloroform in the induction stage, it might be better to teach students to avoid it altogether unless it be directly indicated, and to substitute for it either the ethyl chloride and ether sequence or the use of carbon dioxide as an adjuvant to induction with ether given by the "open" method.

In speaking of tests for anæsthetic tolerance, Dr. Ashworth states that the healthy adult can hold a deep breath for "sixty seconds or more without discomfort". This is surely an over-statement; forty-five seconds would seem a better guide. In dealing with the prevention of respiratory sequelæ, the author discusses the carbon dioxide and oxygen mixture more briefly than it probably deserves. In dental anæsthesia open mask administration is alone described; it is surely time that medical students, dental students and the public at large were taught to expect a better technique.

Apart from such criticisms this little book is sound and informative. It does not set out to replace the student's standard text-books of anæsthesia. It supplements them, however, in many ways. In especial it brings out a wealth of practical points in the care of the patient which are strangely neglected in text-books, but which every student ought to know.

## BLOOD GROUPS AND BLOOD TRANSFUSION.

DR. A. S. WIENER'S book is an excellent presentation of all the important known facts concerning the individuality of the blood and the application of this knowledge to clinical and legal medicine.[1] The chapter on the sources of error in blood grouping is particularly welcome.

Indications for the technique of blood transfusion are given in detail; the reactions are described and the fundamental principles of genetics and biometrics and the heredity of the blood groups are discussed clearly and completely.

The subgroups of groups *A* and *AB* and the importance of the agglutinogens *M* and *N*, of Landsteiner and Levene are given adequate space. References are fairly full and are given at the bottom of the page on which they occur.

The book can indeed be recommended to anyone requiring information on any aspect of blood groups or blood transfusion.

## SEROLOGICAL REACTIONS AND THEIR SPECIFICITY.

IN his book entitled "The Specificity of Serological Reactions", Dr. Karl Landsteiner has given us a fairly extensive review of the observations that have been recorded in an endeavour to throw more light on the nature of antigen-antibody reactions.[2] Although not intended as a book of reference, the bibliography at the end of each chapter renders it a valuable *vade mecum* to all those interested in this branch of immunology.

The chapter dealing with artificial conjugated antigens is excellent and deals with an aspect of the problem to the knowledge of which Dr. Landsteiner has made many contributions. The introduction of substances of known chemical composition into the protein molecule and the production of antisera to these artificial antigens has opened up a very promising field for exploration, and the author has traced the development of this technique during the past decade. Our present knowledge leaves many important questions still in doubt. The specificity observed with some hapten groupings and the numerous cross reactions with others render quite impossible the postulation of a theory of the serum reactions comparable with those covering the phenomena of chemistry.

The subject matter of the book is well arranged, but it is hardly a book through which the student may begin his study of the subject, and in this respect we beg to differ from the author. For those interested in immunology the book is well worth reading, and it contains many suggestions for further work.

[1] "Blood Groups and Blood Transfusion", by A. S. Wiener, A.B., M.D.; 1935. London: Baillière, Tindall and Cox. Super royal 8vo, pp. 234, with illustrations. Price: 18s. net.

[2] "The Specificity of Serological Reactions", by K. Landsteiner, M.D.; 1936. Springfield: Charles C. Thomas; London: Baillière, Tindall and Cox. Royal 8vo, pp. 185. Price: 18s. net.

# Notes on Books, Current Journals and New Appliances.

## A BOOK ON SURGICAL NURSING.

THAT a fifth edition, running into the eighteenth thousand, of Dr. H. C. Rutherford Darling's book on surgical nursing and after-treatment should be called for is an indication of the usefulness of the book and a tribute to its author.[1] The text has been revised in an attempt to include additions to knowledge that should be known to members of the nursing profession. In previous notices of this book it was pointed out that the author has tried to meet the needs of those who sit for the final examinations of the Australasian Trained Nurses' Association. The book deals with surgical nursing only and is divided into two main sections. The first section is devoted to general surgical nursing, and the second to regional surgical nursing. The volume is well illustrated and the printing and general make-up are attractive. We wish the author the further success that his book undoubtedly deserves.

## TREATMENT IN GENERAL PRACTICE.

MANY members of the British Medical Association in Australia have read with appreciation the special articles on treatment that have been appearing in *The British Medical Journal*. Articles of this kind have a definite value, and we recall the many expressions of satisfaction that followed the publication of a series of special articles on diagnosis in this journal. *The British Medical Journal* articles have been contributed, as were our own, by specially selected authors known to have an interest in a chosen subject. Those that appeared between December 8, 1934, and July 27, 1935, have been published in book form.[2] This group of articles is devoted to diseases of the respiratory system, acute infectious fevers and cardio-vascular conditions. The authors are teachers of clinical medicine in various medical schools and write in a practical way "to convey the teaching in clear-cut shape, even to the point of dogmatism". We suspect that even those who keep their journals, as well as those who file articles of interest by the scrap-book method, will be glad to know that these valuable contributions may be obtained in a well-bound volume of a handy size at a moderate cost.

[1] "Surgical Nursing and After-Treatment: A Handbook for Nurses and Others", by H. C. Rutherford Darling, M.D., M.S., F.R.C.S., F.R.F.P.S.; Fifth Edition; 1935. London: J. and A. Churchill. Crown 8vo, pp. 750, with illustrations.

[2] "Treatment in General Practice: The Management of Some Major Medical Disorders", articles republished from The British Medical Journal; 1936. London: H. K. Lewis and Company Limited. Demy 8vo, pp. 258. Price: 8s. 6d. net.

The Medical Journal of Australia

SATURDAY, AUGUST 8, 1936.

*All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.*

*References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: Initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.*

*Authors who are not accustomed to preparing drawings or photographic prints for reproduction, are invited to seek the advice of the Editor.*

## A NEURO-HORMONAL TREATMENT OF CANCER.

In a communication received by air mail from Dr. V. M. Trikojus, of the Department of Medicine of the Medical School, University of Sydney, who is at present working at the Pharmacological Institute at Freiburg, in Breisgau, reference is made to a new treatment of cancer proposed by a group of three workers whose standing justifies a consideration of their claims. These workers are: Professor F. Blumenthal, former Director of the Institute for Cancer Research at Berlin and for many years General Secretary of the German Central Committee for the Investigation of and Campaign against Cancer, now engaged in research work at the Poliklinik for Cancer Patients at Belgrade, Jugo-Slavia; Dr. E. Jacobs, a cancer specialist who treats patients at the Bizêtre and St. Louis Hospitals in Paris; and Dr. Hugo Rosenberg, a research chemist at Basel. In the *Schweizerische Medizinische Wochenschrift* of July 4, 1936, Blumenthal gives the history of his discovery of the treatment, Jacobs discusses its effects on 114 patients suffering from advanced cancer, and Dr. F. Cailliau, Professor of Pathological Anatomy in Rouen, describes his histological researches on the results of treatment.

Researches concerning the effect of extracts from animal organs on the growth of tumours have been in progress since the beginning of this century. In recent summaries of work in this field, such as that of Sannié and Alphandéry (*Bulletin du Cancer*, Volume XXV, 1936, page 122) it is concluded that the hopes of a successful treatment based on these effects have not been fulfilled. Nevertheless the three Basel workers, Blumenthal, Jacobs and Rosenberg, combined forces in 1935 and used as the material for their preliminary experiments extracts from the liver, stomach, pancreas, intestine and spleen of animals immediately after they had been killed in the slaughter-house. Extracts made from these organs were found to exert specific action on cancer tissue. Tests were carried out in the first place on tumour-bearing rats. It was observed that a certain combination of these extracts inhibited the growth of a transplanted rat tumour, whereas a different set of extracts caused fully developed tumours to regress. The success which attended these experiments on rats led the authors to apply the same treatment to human beings afflicted with tumours. It was found that the action on the cancerous growth consisted not in simple destruction of the tumour, but in certain morphological changes, confirmed by the histological examination of the affected tissues by Cailliau. These changes occur in the first place in the nerves and vascular system of the tumour. Impulses from the nerves are held to be transmitted to the reticulo-endothelial system; and these impulses appear to play an important part in the destruction of the growth.

Of the 114 cases of cancer that were treated, all were very advanced, except ten which were skin cancers; in 104 instances the growth had passed the stage at which radiation or surgical treatment could be effective. In these apparently hopeless cases the patients had either primary tumours with metastases or had metastases only, the primary tumour having already been removed by surgical operation. In the course of the new treatment it was observed that the metastases often reacted more

rapidly than the primary tumour, when both were present. In many cases treatment was controlled by means of biopsies which Cailliau made from time to time; in every instance changes in the nervous and in the vascular tissue of the tumour were found to precede its destruction. These changes were specific features of the treatment. Cailliau states that he has never observed them in tumours treated by irradiation. Cailliau's findings indicate that in the Basel treatment specific reactions are called into play, which may finally lead to healing, and that the manner of healing is utterly different from that which occurs in cases successfully treated by irradiation.

Blumenthal emphasizes that it is too early yet to say to what extent the histological cure signifies a clinical cure and how long the cure lasts. He states, however, that health was restored in many apparently hopeless cases and that in many others a great improvement was achieved. In some cases in which the cancer cells appeared to be destroyed morphologically the tumour had not regressed; in other words, there are tumours in which the cancer cells are destroyed, but which do not immediately regress to any appreciable extent. In Jacobs's report of the clinical effects of the polyvalent hormone therapy, as the treatment is called, 78 cases which are of particular interest are grouped as follows: (i) Twelve skin cancers of spinocellular (prickle cell) type or mixed forms, some inoperable, some already operated on, others irradiated for a long time, others recurrent cases. (ii) Nine inoperable cases of cancer of the rectum, several of the patients having an artificial anus. (iii) Nine inoperable intestinal cancers, several patients having an artificial anus. (iv) Ten stomach tumours, some inoperable, some patients having undergone partial gastrectomy and having fistula openings; among these were two patients with liver metastases, one patient with liver and pancreas metastases, one with bone metastases and one with glandular metastases. (v) Eighteen mammary gland tumours, all inoperable or recurrent and all with metastases. Among these, eleven patients had glandular metastases, six had skin metastases, three had metastases of the vertebral column and three had lung metastases. (vi) Eight inoperable uterine and ovarian tumours, some having already been operated on, others recurrent and others again having been irradiated. Among these, three patients had ascites, one had metastases in the vertebral column, two had extension to the rectum and two had extension to the bladder. (vii) Large isolated malignant tumours, inoperable or already operated on, recurrent or irradiated. Among these there were: one pancreas tumour, one tongue tumour, one penis tumour with two stomach tumours the size of a child's head and skin metastases, three œsophageal tumours, three kidney tumours, two bronchial tumours and one brain tumour, only partly removed and twice irradiated. This enumeration shows that most of these were desperate cases in which the patients had nearly all been already operated on or in which irradiation had been carried out. In many cases narcotics were being administered to relieve pain, growths having made their appearance in many parts of the body.

Many of these patients are now in a greatly improved state; some have returned to their normal activities, that is, they no longer have pain or discomfort and have no tumours, so far as can be ascertained. Of the 114 patients, four died; one of these patients had a bladder tumour with uræmia, another had a lung tumour, a third had a stomach tumour with liver and pancreas metastases, the fourth had a stomach tumour with stenosis. All cases were controlled so far as possible during the treatment by blood tests, X ray photographs and at intervals by biopsies. It is emphasized that every other form of treatment directed against the growth, such as irradiation, was abandoned while the present treatment was being applied. Jacobs gives details of the progress of some of these patients; of these only one or two need be quoted. Three patients with cancer of the breast who had been operated on and who were found to have secondary deposits in the vertebral column, and one patient with cancer of the uterus who had metastases of the vertebral column, were relieved of severe pain for which morphine had previously been administered. Three of these patients are now able to walk upright without difficulty, having previously been unable to

remain erect; the fourth is able to move and has no pain, but cannot yet walk with ease; this last patient has been treated for only two and a half weeks. One patient had been operated on for a carcinoma of the penis which had recurred and had been repeatedly irradiated; skin metastases were present and two stomach tumours of the size of a child's head; these tumours could only just be detected after four weeks' treatment. Although in this case the skin metastases had regressed only to a slight extent, no new metastases had formed. This slight response of small skin metastases was also observed in the case of a breast tumour. Another patient who may be specially mentioned had an œsophagus-stomach cancer which had already been operated on three times; the patient, who had been confined to bed for nearly a year, had sunk into a cachectic state, but after treatment recovered sufficiently to return to work.

The treatment itself consists of intramuscular injections accompanied by tablets taken orally; when external ulcerated tumours are present an ointment is also applied. The treatment is painless and generally without particular reactions. The general condition is often affected within a few hours of the first injection. The dosage differs, naturally, for different cases. Three different solutions, *A*, *B* and *C*, are used for intramuscular injection: *A* exerts a strong action on the sensitivity to pain, *B* appears chiefly to affect the metastases, and *C* the primary tumour and general condition. Large doses can be given in the early days of the treatment to patients with severe cachexia. In the case of bone metastases, lung metastases, stomach and rectum tumours, which are often accompanied by great pain, the following treatment was applied: (i) One intramuscular injection in the morning of four cubic centimetres of *A*; in the evening one injection of two cubic centimetres of *B* and two cubic centimetres of *C*, mixed. (ii) Four to six tablets *per diem*. It is often found to be an advantage to introduce pauses of one to four days in the treatment. In cases in which a decrease in the blood pressure results from the action of *A* and *B* it is found advisable to administer preparations of caffein and camphor, or adrenaline. When slight skin tumours are to be treated the ointment and tablets alone often cause the tumours to vanish after a short time without leaving a scar. For deeper epitheliomata injections are necessary. The method is being tried in the University Clinic of Geneva (under Professor Jentzer) as well as in the hospitals mentioned above. The paper by Dr. Cailliau is illustrated by photomicrographs of tissue removed for biopsy. Changes during the treatment are described, particular importance being attached to the observation of neuro-vascular lesions which result from the therapy. This leads Dr. Cailliau to propose a neuro-hormonal theory of the action of the extracts *A*, *B* and *C*.

It is, of course, far too early to pronounce judgement on the efficacy of this treatment. The results so far obtained are unusually encouraging, but many investigators will doubtless be sceptical of such remarkable findings; time alone will show whether the results are short-lived or likely to be permanent. When a record of the cases treated in the important hospitals mentioned is published, an estimate of the treatment will be possible.

## Current Comment.

### BRONCHOSCOPY IN CANCER OF THE LUNG.

From time to time attention has been drawn to the importance of recognizing cancer of the lung at an early stage. The great variability shown by bronchogenic carcinoma in causing metastatic deposits is a feature of this all too common condition, which makes it all the more imperative that an early diagnosis should be attempted, since the hope of relief, slender enough at any time, entirely disappears when the growth has made any headway. Moreover, it is important for the patient's sake that the position should be made plain in suspicious cases, and it is in these that bronchoscopy offers valuable assistance in arriving at the conclusion. This has been pointed out in this journal recently by G. R. Halloran, who has set down his personal experiences in this field, and it is interesting now to read the analysis of 300 cases of bronchial carcinoma by R. Kramer and M. L. Som.[1] These authors have found, like all other experts who do this work, that the bronchoscope is of the utmost service, not only in establishing a clinical diagnosis of cancer of the lung, but also in excluding this

[1] *Archives of Otolaryngology*, May, 1936.

possibility. They realize clearly that a definite diagnosis cannot be made in all cases by endoscopic methods, though in some cases pressure effects may be visible even though no abnormal tissue can be seen. It is, of course, only by microscopic examination of biopsy material that conclusive proof is obtainable.

The questions which Kramer and Som set themselves to answer were in how many cases of bronchial carcinoma biopsy diagnosis was possible, in how many cases afterwards proved to be cancer did even the most skilled bronchoscopy fail, what were the characteristic appearances of bronchial cancer, and what help could be given to the surgeon. For this purpose they analysed 100 *post mortem* specimens and compared the data obtained by bronchoscopy during life. This *post mortem* series, like other work on the subject, shows the frequency of suppurative disease of the lung as a complication; for instance, pulmonary abscess was found in 14 out of 100 cases. The authors also found tuberculous disease in four cases, which corresponds roughly with the usual figures. More significant is their conclusion that a comparison of their *ante mortem* and *post mortem* observations enables them to make a classification of lung cancer into three types—carcinoma of a large bronchus, carcinoma of a branch bronchus, and carcinoma of the parenchyma of the lung. This rough distinction is of value, particularly to the surgeon, as the X ray appearances might fail to give clear indications as to the position of the growth, owing to the association of collapse or inflammation of the lung. From the point of view of the accuracy attained in this work, it may be pointed out that Kramer and Som made a correct histological diagnosis in 74% of their cases. The bronchoscopic appearance observed proved to be rather uniform, in spite of the vastly different anatomical conditions encountered. Stenosis of the bronchus may be caused by the mass of the growth itself protruding into the lumen or by infiltration of the wall of the bronchus. It is in this latter variety that early changes may be overlooked, but it was found that when a suspicious area was noticed in a narrowed bronchus a biopsy of the mucosa at this point might occasionally give conclusive information. Ulceration was also sometimes observed. When the lesion began in a small branch bronchus endoscopic diagnosis was sometimes possible, though in other cases no abnormality of the bronchial tree could be demonstrated. In twenty cases the parenchyma of the lung was involved, and in half these cases nothing abnormal was seen; in the remainder some distortion was detected. Kramer and Som emphasize the importance of an appearance of infiltration in a main bronchus in the early diagnosis of submucosal carcinoma, and point out that this is much commoner than a pedunculated growth and may in its early stages give rise to very little stenosis and show little or no alteration in the X ray shadows of the lungs.

In conclusion it is only right to lay stress on the importance of accurate diagnosis, even when the outlook may not seem promising. The clinician wishes to know whether his patient with suspicious digestive symptoms has a cancer of the stomach, though he is well aware that the outlook from the statistical point of view is anything but good. Similarly, he should wish to establish beyond reasonable doubt the cause of suspicious symptoms within the chest, such as pain or other subjective disturbance, cough, and particularly hæmoptysis. X ray examination of the lungs may make the position clear, but the evidence that can be obtained by a skilled bronchoscopist should not be overlooked.

## THROMBOPENIC PURPURA.

HÆMORRHAGIC diseases are not very uncommon. In fact, if we enlarge the strict meaning of the term we can regard it as including all conditions in which spontaneous bleeding occurs in the skin or mucous membranes. During epidemics of infectious disease general practitioners not infrequently see cases in which petechial eruptions are a feature, and these are not necessarily of great severity. Thus every measles epidemic brings forth its occasional hæmorrhagic eruption, emphasizing the rôle which infection may play in producing that clinical sign known as purpura. These cases are easy from the diagnostic point of view, but the occasional cases seen, especially in children or young people, in which petechiæ appear on the skin or bleedings occur from the mucous membranes, are usually obscure.

W. M. Fowler, in writing on the subject of thrombopenic purpura, traverses the whole subject briefly, but emphasizes in particular the importance of infection in the secondary type.[1] It sometimes happens that when a blood examination is carried out on patients with purpura, no definite abnormality is discovered. There may be no poverty of platelets and no prolonging of the bleeding time; in such cases a capillary fragility may be the explanation of the condition, and this in turn may depend upon some deficiency in the supply or absorption of vitamin *C*, as has been recently pointed out. This is one type of case which does not fall within the category of a definite blood dyscrasia. Another variety of which the same may be said is the infective group, to which Fowler directs attention. In his series of 160 cases he recognized 17 as being of the idiopathic type; of the remaining 143, blood dyscrasias accounted for 81, 6 were due to drugs and similar toxic causes, 12 to liver disease, 19 to miscellaneous causes, and 25 were regarded as being due to infection. Two of the patients in this infective group suffered from infective endocarditis; in the other cases varied conditions were considered to be ætiologically important, such as bronchopneumonia, urethritis, enteritis and infections of the upper respiratory tract. No fewer than 19 of these 25 cases occurred in children under the age

[1] *Annals of Internal Medicine*, May, 1936.

of fourteen years. Fowler also deals with the less common but interesting idiopathic type and, of course, records several cases of successful splenectomy, but he also mentions the need for eradication of septic foci. In the present instance nothing more need be said of this idiopathic group, except to agree with the author in his remarks on the diagnostic difficulties and the importance of accurate investigation and an adequate period of observation and preliminary treatment before so severe a treatment as splenectomy is carried out.

There can be no doubt of the possible importance of the question of infection, in particular nasopharyngeal infection. We do not wish to suffer from an *idée fixée* concerning streptococci in the throat, but when we think of otitis and its complications, of the various rheumatic affections, and of nephritis in their possible connexion with streptococcal infection, we surely shall not be acting under an obsessional influence if we think of the importance of this subject in cases of secondary purpura.

## NEUROSIS.

To attribute a patient's symptoms to neurosis is a simple matter; to justify the diagnosis is not so easy. Were medical practitioners able to follow their so-called neurotic patients through the years, they would possibly get a few surprises and also some shocks to their *amour propre*. At the Hospital of the University of Pennsylvania two patients were regarded as suffering from neurosis, but were found later on to be affected by serious organic lesions. In the first case the patient died of diffuse carcinomatosis, secondary to a carcinoma of the ovary, eight months after a diagnosis of neurosis had been made. The second patient, sent by her family physician with a tentative diagnosis of pulmonary tuberculosis, was nervous and introspective. After careful examination she was regarded as neurotic and was told not to worry about her lungs; twelve months later her lungs were extensively involved by tuberculosis and were the site of multiple cavities. The occurrence of these two cases led to an investigation of the after-history of two hundred and fifty patients who had been branded as neurotic. The result of this investigation is reported by B. I. Comroe, who is Instructor in Medicine at the Medical Clinic of the hospital in question.[1] The report carries so obvious and so salutary a lesson that it may be considered at some length.

Replies which could be considered as having some definite value were received from one hundred (or 40%) of the two hundred and fifty patients. Of the one hundred patients, forty reported that their condition was much better or that they were symptomatically cured. In thirty-four the condition had remained *in statu quo*; two patients were symptomatically worse without the appearance of further diagnostic criteria; in twenty-four instances evidence of organic disease had become manifest since the discharge of the patient from hospital. In this last group the time interval between the patient's discharge from hospital and the discovery of organic pathological change was never more than two years; the average period was eight months. Seven of the patients had died; and death in these cases was attributed to abdominal carcinomatosis, carcinoma of the liver, gastric carcinoma, disease of the coronary arteries, Addison's disease, pellagra, and myocardial degeneration. The pathological conditions from which the remaining seventeen patients were eventually found to be suffering form an interesting and formidable list. They include *diabetes mellitus*, gall-bladder disease, duodenal ulcer, pulmonary tuberculosis, ureteral stone, chronic appendicitis, Buerger's disease, suppurative mesenteric adenitis, cardio-vascular disease with arterial hypertension, renal calculus, uterine myoma, mitral stenosis and toxic goitre. On going through the clinical histories of these patients, Comroe finds records of symptoms "which in most instances might have led to the proper diagnosis". He gives several case histories in full. One example is interesting. A patient complained of upper abdominal and retrosternal pain; she had occasional vomiting. Her medical attendant told her she had gall-bladder disease. She became anxious and emotionally unstable. Examination by X rays and other means revealed no abnormality. The physician in charge accepted some of the husband's statements and suspected a sexual basis for the symptoms; he made a final diagnosis of neurosis. Six months later surgical operation was performed, gall-bladder disease was found, and the patient made a complete recovery. In this instance and in two other cases that are described in some detail, too much attention was paid to the patients' behaviour and to their emotional reactions. The subject is one of great difficulty. As Comroe remarks, organic disease and neurosis may coexist and either may be the forerunner of the other. It would be interesting to argue whether either might in any degree enter into the causation of the other. The art of examining a patient who is suspected of suffering from a functional disturbance is not learned in a day. "It is only by becoming perfectly familiar with the patient's mode of life that the doctor can truthfully evaluate the symptoms and findings in any particular case, and at the same time gain the fullest confidence of his patient, which is often 90 per cent. of the treatment." Comroe thinks that patients are best seen alone and that the medical attendant should listen to the patient's whole story. He makes a useful suggestion when he states that the attendant should inquire whether the patient reads medical literature, and to what extent. Comroe's investigation shows that when a diagnosis of neurosis is made, careful periodical examinations should be carried out at later intervals to exclude the advent of organic disease.

[1] *The Journal of Nervous and Mental Disease*, June, 1936.

# Abstracts from Current Medical Literature.

## THERAPEUTICS.

### Late Ether Convulsions.

R. F. WOOLMER AND S. TAYLOR (*The Lancet*, May 2, 1936) describe four cases of convulsions occurring during ether administration in 1935, with the mode of treatment. The patients all had fever, the weather was hot, and atropine, 0·8 to 0·6 milligramme (one seventy-fifth to one one-hundredth of a grain), had been given. The patients' ages were fourteen, six, thirty-nine and twenty years; three were females. Anæsthesia had lasted from ten to sixty-five minutes when convulsions began. Ethyl chloride was given before two of these anæsthetics. The authors suggest that ether upset the heat-regulating mechanism, atropine stopped sweating and prevented heat loss, and the raised temperature led to heat stroke convulsions. The authors recommend that atropine should be limited to 0·43 milligramme (one one-hundred and fiftieth of a grain) in children and young people with fever in hot weather, that excessive coverings should be avoided, that carbon dioxide and oxygen should be given as soon as twitching begins, and that cold sponges and ice should be applied to the body. If convulsions do not cease within one minute, "Evipan sodium" should be injected intravenously. To combat cardiac failure adrenaline and "Coramine" should be given, and for respiratory failure artificial respiration should be used.

### "Atophan."

W. STRAUB (*Münchener Medizinische Wochenschrift*, January 31, 1936) issues a warning against the danger of the prolonged use of "Atophan". The peg on which his article hangs is a fatal case of chronic "Atophan" poisoning. The patient was a man of sixty-eight years, who had suffered for years from increasing arthritic pain and whose final illness was diagnosed as cancer of the stomach. A *post mortem* examination was not made, but during life urobilinogen was found and also certain liver changes were noted. The patient had taken "Atophan" for years, and in the last three months, when the pain got worse, had consumed 500 tablets, each of 0·5 gramme. The result was acute atrophy of the liver. There was no evidence of gastric cancer. The author points out that this is a typical case and should serve as a warning against the increasing unrestrained misuse of "Atophan" and of "Atophan" compounds, which is calculated to bring into discredit a remedy that is useful and safe, if used properly. "Atophan" has been considered harmless, and the indigestion and loss of appetite which often accompany its use have been looked on as unavoidable. It has gradually become a general antineuralgic and has been found more active as an analgesic and antipyretic, especially in arthritic conditions, than most of the older salicylic preparations. Gout and arthritis differ fundamentally in that the gouty patient uses "Atophan" only during the few days of his acute attack, whereas the arthritic suffers continually and is always dosing himself without reference to his doctor. Thus a patient, such as the author describes, takes 500 tablets, that is 250 grammes, in three months. The time factor is important. In gout, treatment is of short duration and the liver damage is not lasting. But long-continued dosing gives the liver no rest. Unfortunately, the liver makes no protest until the breakdown occurs. This is indicated by jaundice often, and more certainly by the appearance of urobilinogen in the urine. The characteristic of these cases is the sudden breakdown of the liver after months without any symptoms. "Atophan" therapy is a matter for the physician, especially in cases of chronic arthritis; and "Atophan" and its numerous substitutes should not be supplied except on a doctor's prescription. The urine of a patient who is taking "Atophan" should be examined frequently for urobilinogen.

### The Use of Helium in Asthma.

THE therapeutic use of helium is based on its decreased specific gravity in relation to nitrogen, a helium-oxygen mixture being easier to breathe than a comparable nitrogen-oxygen mixture, such as air. When there is obstruction to the movement of air in the respiratory tract, an increased pressure is required to transport air to and from the lungs; the pressure required to transport an 80% helium/20% oxygen mixture under the same conditions is approximately one-half that necessary for air. Alvan L. Barach (*Annals of Internal Medicine*, December, 1935) gives details of the technique of the therapeutic administration of helium and the results in four severe cases of asthma. The purity of the helium employed, the rigid exclusion of nitrogen and the maintenance of the constant percentage proportions of the gases in the mixture—these are points of the first importance. The present high cost of helium makes it necessary to use it economically, and the administration is designed accordingly. Several methods are employed. For short periods of administration a mask of light rubber, fitting tightly to the face, is equipped with two one-inch outlets; one of these is connected to the outside air and has a terminal expiratory flutter valve. The other outlet is connected to a Douglas bag into which the gas mixture is admitted. A heater may be inserted between the bag and the mask. The oxygen tent has been modified for the use of the mixture. Methods for the re-use of helium are being developed, and attempts are being made to establish increased pressure during inspiration with a decrease during expiration. The *status asthmaticus* responded readily to the administration of oxygen-helium mixture for periods varying from five minutes up to one hour, after which the patient had relief for six to eight hours. Three cases of refractoriness to adrenaline responded very quickly to this therapy, and a striking change in the clinical picture was produced. Acute attacks of asthma were not aborted by helium. The persistence of asthma of variable degree, particularly in those instances in which adrenaline has failed to give complete relief or lasting benefit, is regarded as the indication for the use of helium in the way described. The gas mixture has also been used in cases of tracheal and laryngeal obstruction.

### Treatment of Gastric Allergy.

H. THIERS AND R. CHEVALLIER (*La Presse Médicale*, May 2, 1936) discuss the treatment of gastric allergy and erosive gastritis by the substance obtained after ultrafiltration of the food causing the allergy. The authors state that it is a question whether the protein which causes an allergic state produces this condition in its original state, or after some change has taken place in it, for instance, does milk act in certain persons as an allergic substance or is it a secondary product due to gastric, pancreatic or intestinal digestion of milk. It is admitted that some substances ingested act so rapidly in causing allergy, that it is unlikely that they can undergo any change; also that on intracutaneous injection some foods cause local or general allergy without undergoing any change after injection. Nevertheless most foods which cause allergic symptoms, epigastric cramps, vomiting, general urticaria or violent malaise do not produce the effect for half to one hour. This time might be necessary for the elaboration of some secondary products from the ingested food. The authors fed allergic subjects with the substance to which they were sensitive, for example, boiled milk or egg; one hour later the gastric contents were withdrawn by tube, centrifuged and passed through ultrafilters. The resultant filtrate contained amino-acids and a ferment and was of complex composition. This ultrafiltrate was found on injection to have an effect in desensitizing the individual against the specific protein which caused his allergic symptoms. Similar good effects were obtained by the injection of this ultrafiltrate in patients with peptic ulcer. Approximately twenty injections were given in each case.

### "Coramine."

P. G. SCHUBE (*The New England Journal of Medicine*, May 7, 1936) describes a study of the use of "Cora-

mine" in dealing with the effects of barbituric acid derivatives. Deep coma and death result sometimes from the use of barbiturates given either therapeutically or as anæsthetics or taken with suicidal intent. Twelve grains of "Sodium amytal" were given by mouth to twenty-four males varying in age from sixteen to fifty-five years, all physically normal. When these patients were asleep, attempts were made to rouse them by shaking and pin-pricking. If they did not become conscious, five cubic centimetres of "Coramine" were given intravenously; if consciousness had not been restored after ten minutes, five cubic centimetres of "Coramine" were administered every ten minutes until the patient was roused. Eighteen of the twenty-four patients were relieved of their symptoms by five cubic centimetres of "Coramine", four required ten cubic centimetres, and two fifteen cubic centimetres. After seven and a half grains of "Sodium amytal", given intravenously, five to ten cubic centimetres of "Coramine" were required to rouse patients from their unconscious state. Similar experiments were made with: "Luminal", six grains given by mouth; "Sodium luminal", six grains given intravenously; "Sodium ortal", nine grains given by mouth; "Nembutal", three grains given by mouth; all in this series were relieved by five cubic centimetres of "Coramine". After seven and a half grains of "Nembutal" were given intravenously, ten cubic centimetres of "Coramine" were required; and fifteen grains of "Nembutal", given *per rectum*, necessitated fifteen to twenty cubic centimetres of "Coramine" to relieve the symptoms. "Coramine" relieved unconsciousness and caused quicker and deeper respirations; hiccup and projectile vomiting occurred in some cases after five to ten cubic centimetres of "Coramine", but no other ill-effects were noted.

## NEUROLOGY AND PSYCHIATRY.

### Magnesium Sulphate in the Treatment of Epilepsy.

ALEXANDER WOLF (*The Journal of Neurology and Psychopathology*, January, 1936) has based his experimental therapy of epilepsy on the knowledge that when the blood magnesium is elevated to excess, it produces coma; that a moderate rise in the blood magnesium will produce drowsiness; and that this sedative effect can be used to control uræmic and eclamptic seizures. A condition analogous to parathyreoid tetany develops when the blood magnesium is pathologically depressed, although there is no change in the blood magnesium in animals after removal of the parathyreoid glands. The method which the author devised for the control of the epileptic seizures was the administration of magnesium in doses large enough to raise the blood magnesium, but too small to produce dehydration. Epsom salt was given to each patient in amount just insufficient to produce a watery motion. A number of other epileptics were given daily doses of mineral oil only as a control. The dose of Epsom salt was given with an eight-ounce draught of water; and there was no restriction of fluid intake. The normal average value for blood magnesium is 3·61 milligrammes; that for epileptics is 3·47 milligrammes. It was found that 58% of the cooperative epileptics improved by a small, daily, non-dehydrating dose of magnesium sulphate. There was no correlation between the degree of improvement and the quantity of Epsom salt given. Three patients with a low blood magnesium content failed to respond to this treatment, and it is therefore concluded that magnesium in small daily doses is effective in some cases neither by filling an elemental deficiency nor by dehydration.

### Vitamin Administration in Dementia Præcox.

J. NOTKIN *et alii* (*The American Journal of Psychiatry*, January, 1936) have carried out an empirical study of the use of vitamins *A* and *D* in a group of patients suffering from *dementia præcox*; they checked their findings with control studies. There were fifteen females and seventeen males, with an equal number of controls. The vitamin preparation was biologically standardized and it was given in combination with a mineral mixture containing 0·45 gramme (seven and a half grains) of calcium and phosphorus. Biochemical determination was made at the beginning and end of observation. One male and one female patient recovered sufficiently to be discharged from hospital; the condition of two males and two females was improved. The remainder showed no change. The authors doubt whether the vitamin-mineral administration could be held responsible for the beneficial results that were obtained. No change was noted in the control groups and no definite changes in the blood biochemistry were noted.

### Dietary Deficiencies and Neuritic Syndromes.

OSMAN C. PERKINS (*The Journal of Nervous and Mental Disease*, May, 1936) reviews an extensive literature showing that dietary deficiency is associated with the ætiology of polyneuritis and presents a survey of eighty-two cases which have come under his own observation. In this series, while multiple neuritis was the outstanding clinical entity, together in some instances with mental symptoms, every patient presented well marked digestive disturbances. Prominent gastric upset appeared in the case histories as indicated by the absence or diminished secretion of free hydrochloric acid, loss of appetite, nausea and vomiting, and diarrhœa. The author propounds the theory that certain people may have a low requirement for vitamins, which would explain why some alcoholics develop neuritic symptoms, and others, taking equal quantities of alcohol, do not. When neuritis is associated with malignant disease of the digestive tract, food intake is faulty and assimilation is disturbed. The varieties of clinical syndromes presented in these cases closely approximated to those seen in such deficiency diseases as beri-beri, pellagra and sprue, which are accepted as due to some avitaminosis. Improvement of the neuritic syndromes occurred when the patients were placed on a high vitamin diet, especially on vitamins $B_1$ and $B_2$. The author further suggests that in patients exhibiting disease of the nervous system in which the pathological change is degenerative and not inflammatory more attention might profitably be paid to dietary deficiencies.

### The Vegetative Nervous System in Dementia Præcox.

WULF SACHS (*The South African Journal of Medical Sciences*, March, 1936) presents an investigation of the vegetative nervous system in one hundred cases of *dementia præcox*. He carried out about fifty tests on each patient and tabulates in detail the results obtained in eighteen cases, which include examples of the hebephrenic, catatonic and paranoid groups. He shows that the state of the vegetative nervous system fluctuates in accordance with the mental state of the schizophrenic. He points out also that the majority of the long-standing chronic cases show a picture of so-called irreducible hypotonia of the vegetative system. He finds the greatest changes in the vegetative nervous system in those patients in whom the dynamic conflict with the external world of reality has not entirely ceased, and again when the patient is acting under the influence of delusions and hallucinations. The author's findings of pronounced hypertonia of both sympathetic and parasympathetic systems in such cases are contrary to those of Claude and others who have investigated this subject. Although he carried out a greater number and variety of tests than any other investigator whose work has been published, he is unable to draw definite conclusions as to the diagnostic or prognostic value of such tests. The behaviour of the catatonic is still incomprehensible. All that can be said of catatonic rigidity is that, from the point of view of reflexes, it is a generalized inhibition, and from a psycho-analytical standpoint, a reaction to endangered repressions. In the paranoid forms of *dementia præcox* the pattern of the disease is too complicated to enable a satisfactory relationship to be established between the mental status and the tonus of the vegetative nervous system.

# British Medical Association News.

## SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held at the Royal Prince Alfred Hospital, Camperdown, on June 4, 1936. The meeting took the form of a series of clinical demonstrations by the members of the honorary staff.

### Phrenic Paralysis.

DR. KEMPSON MADDOX showed a woman, aged fifty-five years, who complained of pain in the chest following an operation three or four years previously in another hospital, where she was told she had pleurisy. She complained of palpitation and dyspnœa, especially when she hurried or became excited. The pain was very troublesome at night; it was situated in the upper part of the thorax, on the left side, and she had to sit up to obtain relief. The pain was in the left diaphragmatic distribution, over the left deltoid and clavicular region. She had a fairly healthy appearance; vocal fremitus, vocal resonance and breath sounds were all greatly lessened at the left base.

The X ray report was that the stomach and duodenum were normal; there was no sign of diaphragmatic hernia; the left dome of the diaphragm was elevated and there was no appearance in the thorax to account for this. It was thought that a subphrenic lesion might be present. The patient had, however, experienced no abdominal symptoms at any time. An investigation was undertaken to exclude the presence of a subphrenic hydatid cyst; the Casoni test gave no reaction, and the leucocytes numbered 10,230 per cubic millimetre, the relative count being normal.

Dr. Maddox remarked upon the similarity between this appearance and that seen after phrenic evulsion, and suggested that in this case possibly the phrenic nerve had become involved in the pleurisy noted in the patient's early history. The possibility of a further subphrenic lesion could be investigated by the production of a pneumoperitoneum. Search by bronchoscopy and bronchography for a bronchial carcinoma causing collapse of the lower lobe would also be undertaken.

### Rheumatoid Arthritis Treated by Gold Injections.

Dr. Maddox also showed a woman, aged forty years, who had had rheumatoid arthritis for four years. The feet, spine, jaws, knees and wrists were chiefly affected. The teeth and uterus had been removed. On December 28, 1935, "Solganol B" injections were commenced; a cloud of albumin appeared in the urine and the "Solganol B" was stopped. The joints were then manipulated under "Evipan" anæsthesia. On January 6, 1936, the patient complained of swelling and pain in the right knee; massage and hot air were commenced. On January 21, 1936, the urine was clear, but pain was still present. Commencing with 0·1 gramme, "Solganol B Oleosum" injections were repeated every week until the full dose of 0·5 gramme was given. On March 10, 1936, the patient was feeling much better. On May 26, 1936, her condition was still improving and no spontaneous aching remained.

Dr. Maddox pointed out that the patient could turn her head completely to either side, knit and sew, do her hair and housework without pain. Some deformity remained, but the appearance of the skin had improved considerably, and she expressed herself as feeling better than she had felt for five years.

### Early Leontiasis Ossea.

Dr. Maddox's third patient was a woman, aged sixty years. This patient had presented herself for treatment for a villous arthritis of the knees, but it was noticed at the time that she had tumour on the right temporal region, which was hard, not definitely circumscribed, and embedded in the temporal muscle; it was probably attached deeply to the zygoma. It was clinically considered to be a metastatic deposit in the temporal bone, though no primary growth could be found.

An X ray examination of the skull was made by Dr. Sear, who reported the presence of sclerosis of the right temporal bone. The appearance, in Dr. Sear's opinion, was that of *leontiasis ossea*. The uniformly dense opacity was limited entirely to the one bone. The orbits were clear. No treatment was contemplated.

### Case for Diagnosis.

Dr. Maddox's last patient was a male, aged fifty-four years, who had complained in 1929 of right facial palsy of three months' duration. In 1934 there was sudden onset of diplopia with slight headache; occasional transient attacks of dizziness and tinnitus had been present in the preceding four months and some dimness of vision for the same period. There was no disturbance of sensation or of movement, no speech changes, no disturbance of micturition or defæcation.

An examination revealed paralysis of the left external rectus muscle; right facial palsy with some muscular twitching was present; the fundi were normal, except for slight cupping of both disks; abdominal reflexes were absent; the right plantar response was doubtful, the left was extensor. The cerebro-spinal fluid was clear, of normal pressure and contained no increase of cells; the Wassermann test gave no reaction; the systolic blood pressure was 160 and the diastolic pressure 100 millimetres of mercury. The radial vessels were thickened, and X ray examination of the chest failed to reveal the presence of a neoplasm. The patient was discharged from hospital with a diagnosis of Bell's palsy (right) and possibly disseminated sclerosis.

In 1936 there was sudden onset of diplopia, associated with pain behind the right eye, but no other symptoms. Examination revealed paralysis of the right rectus muscle, but no involvement of other extrinsic muscles of the eye and no nystagmus. The pupils were normal; the fundi were normal, except for slight cupping of both optic disks. Right facial palsy was present; the abdominal reflexes were absent, and the plantar reflexes were both flexor. No ataxia of either upper or lower limbs was present. The systolic blood pressure was 218 and the diastolic pressure 130 millimetres of mercury. The blood did not react to the Wassermann test. The suggested diagnosis was: disseminated sclerosis, cerebral arteriopathy or intracranial neoplasm.

### Epituberculosis.

DR. A. W. MORROW said that a child affected by epituberculosis was young, ailing perhaps, but not ill. Fever was slight or absent. Sputum, if obtainable, was not found to contain tubercle bacilli. The Mantoux test usually gave a positive reaction. The physical signs suggested consolidation, and the radiological picture showed a homogeneous shadow, as a rule involving one lobe and usually an upper lobe. Recovery generally occurred.

Suggested causes were as follow: (i) Collapse of a lobe or part of a lobe due to pressure of a tuberculous gland or a bronchus (Scott Pinchin and Morloch). (ii) Non-tuberculous infiltration around a tuberculous gland, the condition being looked upon as an allergic manifestation. (iii) Tuberculous infiltration (J. C. Spence). (iv) Unresolved pneumonia. The absence of cough and sputum or any tendency to bronchiectasis would appear to exclude this suggestion.

Dr. Morrow showed a girl, aged twelve years, whose sister suffered from pulmonary tuberculosis; the patient had reported for examination as a contact. She had had a slight cough without sputum for some weeks, but did not feel ill and had continued at school. Examination revealed a child somewhat pale, with a slightly impaired percussion note in the right interscapular fossa and diminished breath sounds in this zone. Radiographically she appeared to have some consolidation of the right middle lobe of the lung. Her temperature was 37·4° C. (99° F.). The Mantoux test gave a strongly positive reaction. The child had been instructed to remain away from school and to rest at home for two weeks and then to report back at the dispensary. One month later she was thoroughly well and radiographically the lesion had disappeared.

### Tuberculous Empyema.

Dr. Morrow said that the development of tuberculous empyema presented one of the major problems in collapse therapy in the treatment of pulmonary tuberculosis. He showed two patients to demonstrate this complication and, furthermore, to demonstrate the fact that, despite the presence of purulent material in the pleural sac, the patients were able to live a restricted existence as outpatients. "Metaphen", a pleural antiseptic, was being used at the moment in both these patients, five cubic centimetres of a 1 in 500 solution being injected into the pleural sac each week. It was too early to make any observations on the effect of this therapy, but no doubt surgical treatment would be necessary before a cure was obtained. Both patients were under the direct care of Dr. F. W. Clements, as he was carrying on some investigations into the cause of pleural effusions in artificial pneumothorax.

The first patient was a male, aged forty-three years, who had had pneumothorax induced at another institution fourteen months previously for unilateral pulmonary tuberculosis (left side). The patient was admitted to the dispensary four months before the meeting with left-sided hydropneumothorax. Two months before the meeting the fluid was found to be purulent; it contained tubercle bacilli. Treatment with "Metaphen" was commenced, together with aspiration. Tubercle bacilli were still present in the fluid. The patient's weight had fallen from 71·7 kilograms (eleven stone five and a half pounds) to 69 kilograms (ten stone thirteen and a half pounds); the temperature had not been above 37·5° C. (99·6° F.).

The second patient was a male, aged thirty-two years, who had had artificial pneumothorax performed on the right side for unilateral pulmonary tuberculosis at another institution on April 3, 1935. He was admitted to the dispensary on September 25, 1935, with hydropneumothorax (right side). Turbid fluid was aspirated on November 21, 1935, and February 21, 1936.

Treatment with "Metaphen" was commenced on April 15, 1936. The fluid contained the tubercle bacillus and the *Staphylococcus aureus hæmolyticus*. At the time of the meeting the fluid contained only the tubercle bacillus. The patient's weight had varied from 67 kilograms (ten stone nine pounds) to 70·2 kilograms (eleven stone two pounds) and now he weighed 63·4 kilograms (ten stone one pound). His temperature had never been above 37·1°·C. (98·8° F.).

### Œsophageal Obstruction.

DR. GARNET HALLORAN presented for differential diagnosis a series of cases in which œsophageal obstruction was the predominant symptom.

#### *Plummer-Vinson Syndrome.*

A female patient, aged fifty years, complained of a feeling of suffocation in the throat with slight dysphagia. She could swallow solids slowly. Partial gastrectomy had been performed several years previously. Glossitis and longitudinal striation of the nails were observed. Examination by direct œsophagoscopy and by X rays revealed no abnormality of the œsophagus. A fractional test meal revealed a severe hypochlorhydria, only traces of free hydrochloric acid being found. The blood count revealed a hypochromic and microcytic anæmia. The figures were as follows: red cells, per cubic millimetre, 4,530,000; hæmoglobin value, 58%; colour index, 0·66; hæmatocritic reading, 32%; mean corpuscular volume, 71 cubic microns; mean corpuscular hæmoglobin, 20 micro-microgrammes; mean hæmoglobin concentration, 29%. Massive doses of iron and dilute hydrochloric acid were prescribed.

#### *Œsophageal Hernia at the Diaphragm.*

A female patient, aged fifty-eight years, had complained for four and a half years of obstruction to food at the epigastrium. A few minutes after being swallowed the food would pass on to the stomach. When obstruction was severe, pain was felt from the sternum to the scapulæ. Much of the food was vomited, and 3·6 kilograms (eight pounds) in weight had been lost in two months. Cardiospasm had been wrongly diagnosed from the X ray picture, but a later radiological report stated that there was an œsophageal orifice hernia of the congenitally short œsophagus type. This filled, as was usual in these cases, only when the patient was in the prone position; it could not be seen at all when the patient was in the erect position. There was no delay in the passage of the meal down the œsophagus, and no organic lesion of the œsophagus itself could be detected.

Direct œsophagoscopic examination revealed a slit-like orifice twelve and a half inches from the upper incisors. It was not ulcerated, was permeable and dilatable, and did not appear malignant. A diagnosis of œsophageal hernia or pouch was made. For a year this patient had passed œsophageal bougies on herself up to size 34 French, but pain prevented further dilatation. She gained weight and looked well, but still suffered from some degree of obstruction and indigestion, although her life was much more comfortable.

#### *True Cardiospasm.*

A female patient, aged thirty-nine years, had suffered from pain and difficulty in swallowing solids for five years and was losing weight. X ray examination revealed the typical dilatation of a cardiospasm. Direct œsophagoscopy showed the whole œsophagus to be greatly dilated, the mucosa being very rugose and retained food being present. The cardiac orifice was dilatable. There was no evidence of malignancy or other stricture, and the appearances were typical of cardiospasm.

#### *Gastric Carcinoma Simulating Cardiospasm.*

A female patient, aged fifty years, complained of dysphagia and vomiting which had increased over a period of seven months. She had lost 18·9 kilograms (three stone) in weight. An X ray picture demonstrated very marked obstruction at the lower end of the œsophagus with great dilatation of the latter; though the lower end was fusiform, as usually seen in cardiospasm, the narrowing was slightly higher and more irregular than in cardiospasm. The appearance suggested ulceration or neoplasm supervening on cardiospasm. Direct œsophagoscopy revealed a normal cardiac orifice fourteen and a half inches from the upper incisor teeth. There was no infiltration and no broken mucosal surface and no evidence of malignancy. The liver tunnel was patent. A diagnosis of cardiospasm was made.

At a later date large size mercury bougies were easily passed into the stomach and great improvement in swallowing resulted. One month later loss of weight continued and the fluoroscopic screen revealed that the bougies were no longer entering the stomach. A provisional diagnosis of neoplasm was made. Exploratory gastrostomy revealed carcinoma of the fundus surrounding the cardiac orifice and fungating posteriorly within the stomach. No glands were felt. The patient was shown to illustrate the difficulty of making a differential diagnosis in such cases, which were not uncommon.

#### *Tertiary Syphilitic Stricture of the Œsophagus.*

A male patient, aged sixty-one years, had complained of œsophageal obstruction with much loss of weight for six months. Clinically his condition resembled that seen in *carcinoma œsophagi*. The X ray report stated that there was a constriction at the lower end of the œsophagus, near the cardia, about one and a half inches in length, not typical of malignant disease. Direct œsophagoscopy revealed a smooth fibrotic stricture nine and a half inches below the upper incisor teeth. It did not resemble a neoplasm, but suggested tertiary syphilitic fibrosis. The reaction to the Wassermann test was found to be triple positive. Suitable antisyphilitic treatment and autodilatation prevented further constriction of the gullet.

A female patient, aged fifty-two years, had complained for several months of increasing dysphagia. When she was first seen even liquids could not be swallowed. The X ray report stated that there was stricture of the œsophagus at the level of the seventh and eighth thoracic vertebræ, almost certainly due to neoplasm.

Direct œsophagoscopy confirmed the X ray diagnosis and a biopsy specimen revealed squamous-celled carcinoma. The stricture was dilated and a full-sized Souttar's tube placed therein. This patient lived for one year and ten months after intubation. Œsophagoscopy was performed three times during this period to remove particles of unmasticated food or to replace the Souttar's tube, and gastrostomy was never necessary.

### Carcinoma Vulvæ.

DR. CLEMENT CHAPMAN showed two cases of *carcinoma vulvæ*. The first patient had a history of *pruritus vulvæ* associated with leucoplakia of twelve years' duration. Two local excisions of ulcerated areas had been performed six and four years previously. There was present at the time of the meeting extensive leucoplakia of the whole vulva extending to the *mons veneris* and to the inner aspect of the thighs with fissuring of the anterior margin of the anus. On the inner side of the anterior third of the left *labium minus* was a typical epitheliomatous ulcer of four centimetres diameter, still operable. There were no glands palpable in either the inguinal or femoral region. The patient had glycosuria. It was therefore proposed to give a complete course of deep X rays while she rested in bed. Four weeks after completion of this treatment block dissection of vulva and regional glands was to be performed.

The second patient had a similar history of leucoplakia of ten years' duration, ending in a carcinoma of the clitoris. She had been treated by a like method eight months previously. Her health was good and there was no sign of recurrence nor any inconvenience.

Dr. Chapman stressed the fact that in his experience *leucoplakia vulvæ*, once it had ulcerated, always progressed to cancer. In such cases limited local excisions should not be performed, but the whole affected area should be removed at once. Radium treatment by needling was local and therefore always inadequate.

### Cerebellar Tumour.

DR. A. T. NISBET showed two patients who were suffering from cerebellar tumour.

The first was a man, aged thirty-five years, who had complained in November, 1931, of headaches and morning vomiting; his eyesight had rapidly failed during the previous ten days, and at the time of the original examination it was very difficult for him to read. In addition, giddiness had occurred at spasmodic intervals. There was no previous history of illness, except scarlet fever sixteen years before.

On November 17, 1931, Dr. Poate performed a craniotomy in the right occipital area. There was considerably increased intracranial pressure. The *dura mater* was exposed and excised, the sagittal sinus tied and divided, and the right lobe of the cerebellum was explored for a tumour. Suspected tumour tissue was seen very deeply in this area of the brain, but it was not considered advisable to remove any of it.

On December 1, 1931, the patient was brought to the radiotherapy department on a stretcher, unable to stand, with a nystagmus and double vision. A full course of X radiation was given, which lasted until February 24, 1932. The patient improved rapidly, and three months later was allowed to return home to the country. Twelve months later he was capable of driving a motor car and walking up to a mile and a half. Six months later he returned to his old occupation as boundary rider, and since that date had been daily in the saddle.

A second course of irradiation was given in 1932, purely on account of the patient's satisfactory condition, and as an attempt to prevent any recurrence. Dr. Nisbet said that this patient had come to the meeting by himself a distance over two hundred miles and intended to return home next day.

Dr. Nisbet's second patient was a girl, aged fourteen years, who in May, 1932, had a craniotomy performed by Dr. Poate, when it was found that there was extreme intracranial pressure and that the right lobe of the cerebellum bulged into the surgical opening. Profuse bleeding prevented exact localization of the tumour.

Nearly twelve months later this patient was sent to the radiotherapy department, as symptoms had considerably increased. At this time she had continual headaches, numbness over both sides of the face and in the upper part of both arms. The tongue was numb and practically immovable and pain was present in the right ear. A full course of radiation was commenced immediately. The patient, as could be seen, had grown into a tall, good-looking young woman with all her mental faculties. The only symptom at the time of the meeting was a dimness of vision of the left eye, which had become no worse during the last twelve months.

Dr. Nisbet said that he considered these two cases to belong to the group of cerebellar medulloblastomata, which had proved to be exceedingly sensitive to radiotherapy. He referred to an article in the *American Journal of Roentgenology* of April, 1936, in which E. C. Cutler and others considered that irradiation was the most hopeful form of therapy in the possible cure of this type of neoplasm.

*(To be continued.)*

## NOMINATIONS AND ELECTIONS.

THE undermentioned have been elected members of the Victorian Branch of the British Medical Association:

Newbold, Vivienne Mary, M.B., B.S., 1935 (Univ. Melbourne), Royal Melbourne Hospital, Melbourne, C.1.

Jones, Lorna Doreen, M.B., B.S., 1931 (Univ. Melbourne), 300, Grange Road, Ormond.

# Correspondence.

## BRONCHIECTASIS.

SIR: Repeated discussion of the subject of bronchiectasis by several scientific bodies recently and the space that consideration of this subject has been afforded in your valuable pages are evidence of an awakening in the profession to the importance of this crippling disease. But it must be stated forcibly that the attention devoted to bronchiectasis among hospital special departments is not so evident among general practitioners.

The disease is by no means restricted to patients of the hospital class. And every doctor will do well to look out for cases, particularly among his young patients.

Yours, etc.,

E. P. BLASHKI.

Hengrove Hall,
193, Macquarie Street,
Sydney,
July 9, 1936.

## MITHRIDATISM.

SIR: I have been very interested in the latest discussions on nicotine, because the affirmation by a German authority that one cigar or five cigarettes contain enough nicotine to kill a man is everywhere derided, or at least politely not believed by a large number of doctors and by people in general who smoke a great deal—and nobody dies of nicotine poisoning.

However, every medico-legal or toxicologist world's authority can positively and scientifically state that nicotine is very, very poisonous, something like strychnine and potassium cyanide, the mortal dose of strychnine being from one-quarter of a grain (16 milligrammes) to one grain (64 milligrammes) and of the cyanide and nicotine being about one grain (64 milligrammes).

There have been many cases of death by nicotine poisoning, like that Sydney woman who died in the year

1902 twenty minutes after a quack had administered an enema consisting of an ounce and a half of tobacco in a quart of water; and also there have been reported in other countries deaths from administering only a very small quantity of strong tobacco, as two grammes. A mild 10% solution of nicotine kills the *Bacterium coli* in about fifteen minutes, and tobacco smoke rapidly destroys the cholera vibrio and the *Diplococcus lanceolatus* of pneumonia.

The contents of nicotine in tobacco is from 0·5% to 5·0%. Pipe mixtures contain the largest amount of nicotine (2·04% to 2·85%); Egyptian, Turkish and Virginian cigarettes come next with 1·38% to 1·80%. A mild British cigar contains less than 1·24%, and a Havana cigar least of all with 0·64%. But in tobacco with the nicotine there are also furfural (harmful substance), especially in the cheap Virginian cigarettes (not present in cigar and pipe tobacco), ammonia, and pyridine (very potent poisons, but only about one-tenth of the quantity of the nicotine). The furfural, ammonia and pyridine are responsible for the irritating effect on the throat.

Each individual has a different natural physical resistance against different poisons. For instance, each one of us has a different resistance to any physical straining, as hard manual work, foot running, jumping, swimming, fighting, eating or drinking *et cetera*, and each individual obtains better resistance with training in any physical strain, as well as resistance to any poison, such as nicotine, for we have the very, very old law of the mithridatism: a kind of acquired poison-proof, from gradually increasing doses of toxic and poisonous substances. Mithridates the Great (134 B.C. to 63 B.C.), king of Pontus in the Black Sea, Asia Minor, was the discoverer of the above facts. He tried to inure his own body to particular poisons. From his marvellous ideas and experiments great knowledge was acquired, so that today, after more than 2,000 years, these different grades, commonly known as poison habit, poison resistance or poison-proof, are still universally called mithridatism.

Every medical man in his day's work has to face this mithridatism in treatment of patients, when medicines, drugs and poisons have often to be increased or suspended or changed because the patient has become used to them and he does not get the desired effect. For instance, nervous patients get good, sound sleep at nights at first with mild doses of bromides, but after a few days or weeks those mild doses lose their effect and must be increased, sometimes enormously, or other drugs, such as "Luminal" *et cetera*, must be given. Practically speaking, this mithridatism is one of the greatest assets of marvellous Mother Nature for defending us against poisons.

The writer in 1926, then an interne in one of the clinics of the Royal University of Genova, in order to demonstrate that strychnine has no cumulative action, carried out some interesting research experiments on himself. Starting to take by mouth two milligrammes (one thirty-second of a grain) of *Strychninæ Nitras* every day, in two months increased the dose to 10 milligrammes (one-sixth of a grain) a day, and took this quantity for two months, after which time he increased it to 12 milligrammes (one-fifth of a grain) for a few weeks, thus demonstrating that if strychnine had cumulative action the writer should have been dead when every three days he was taking enough of this poison to kill an average person. But as a result of the acquired mithridatism he did not die, nor did he feel very sick.

Mithridatism, in my opinion, is the explanation of people taking poison without dying, when they are taking poisons for a long time and getting used to them; and with special regard to tobacco smoking and nicotine, abused by a number of people without death, we can very easily explain it on account of: (i) scientific research and medical observations regarding normal animal tissues having the power to destroy (by ferment action and not by chemical combination with the tissues) a certain quantity of the alkaloid nicotine; (ii) the same normal animal tissues which have been rendered tolerant to nicotine becoming able to destroy a considerably larger amount; (iii) the biggest percentage of the nicotine going out in the smoke and in the air without affecting the smoker; (iv) and a lot of it remaining in the "butts"; so that (v) a very, very small percentage is really intoxicating the smoker, and the smoker becomes used to that very small percentage because of the above-mentioned mithridatism. So that, in conclusion, nobody dies from smoking tobacco, despite the fact that a cigar weighing six grammes, or five cigarettes containing 5% nicotine kills, if eaten, the average person of about ten stone weight or less.

Yours, etc.,

A. B. VATTUONE, M.D.

113, Wickham Terrace,
Brisbane,
June 10, 1936.

## WYNDHAM FLYING DOCTOR.

SIR: We wish to direct attention to the advertisement at present appearing in the journal for a medical officer at Wyndham, Western Australia.

By special arrangements with the Department of Public Health the medical officer at Wyndham also acts as flying doctor for Australian Aerial Medical Services. The Wyndham base is maintained by the Victorian Section, which has a contract with the MacRobertson Miller Aviation Company. The 'plane is named "Dunbar Hooper" after the late Dr. J. W. Dunbar Hooper, of Melbourne, and the pilot, Mr. Robinson, is one of the most capable in the north-west.

Dr. Coto, who completes his term shortly, has set a high standard as the first flying doctor and some of his flights already rank as epics in aviation history.

In the first year of operation sixteen flights (6,500 miles) were made.

The wireless station to be erected next month will greatly increase the scope and interest of the work.

Australian Aerial Medical Services is taking steps to secure full recognition of the valuable work done by its flying doctors and hopes soon to be able to give assistance in post-graduate study after completion of satisfactory term of service. Premium is paid on an insurance policy for £1,000 to cover loss of life while flying, and other benefits.

Full particulars may be obtained from the offices of Australian Aerial Medical Services, Sydney, Perth or Melbourne.

Yours, etc.,

J. NEWMAN MORRIS,
President,
A.A.M.S. (Victorian Section).

Scott's Hotel Building,
434, Collins Street,
Melbourne, C.1,
July 28, 1936.

## Books Received.

DISEASES OF THE EYE, by J. H. Parsons, C.B.E., D.Sc., F.R.C.S., F.R.S.; Eighth Edition; 1936. London: J. and A. Churchill Limited. Demy 8vo, pp. 713, with illustrations. Price: 18s. net.

APPENDICITIS: WHEN AND HOW TO OPERATE: A GUIDE FOR THE GENERAL PRACTITIONER, by W. J. S. McKay, M.B., M.Ch., B.Sc.; 1936. Australia: Angus and Robertson Limited. Demy 8vo, pp. 270, with illustrations. Price: 12s. 6d. net.

PHARMACOPŒIA AND GUIDE OF THE SCHOOL OF TROPICAL MEDICINE AND CARMICHAEL HOSPITAL FOR TROPICAL DISEASES, CALCUTTA; 1936. Calcutta: Art Press. Demy 18mo, pp. 164.

CYSTOSCOPY AND UROGRAPHY, by J. B. Macalpine, F.R.C.S.; Second Edition, revised and enlarged; 1936. Bristol: John Wright and Sons Limited. Demy 8vo, pp. 491, with 297 illustrations in the text and 14 coloured plates. Price: 30s. net.

SALTS AND THEIR REACTIONS: A CLASS-BOOK OF PRACTICAL CHEMISTRY, by L. Dobbin, Ph.D., and J. E. Mackenzie, D.Sc.; Sixth Edition; 1936. Edinburgh: E. and S. Livingstone. Demy 8vo, pp. 255. Price: 6s. net.

THE DIABETIC LIFE: ITS CONTROL BY DIET AND INSULIN: A CONCISE PRACTICAL MANUAL FOR PRACTITIONERS AND PATIENTS, by R. D. Lawrence, M.A., M.D., F.R.C.P.; Ninth Edition; 1936. London: J. and A. Churchill Limited. Demy 8vo, pp. 239, with illustrations. Price: 8s. 6d. net.

VITALITY AND ENERGY IN RELATION TO THE CONSTITUTION, by T. E. Hammond, F.R.C.S.; 1936. London: H. K. Lewis and Company Limited. Demy 8vo, pp. 326. Price: 12s. 6d. net.

THERAPEUTIC USES OF INFRA-RED RAYS, with a Chapter on the Treatment of Sinusitis by Radiotherapy, by W. A. Troup, M.D., Ch.B., with a foreword by Sir William Willcox, K.C.I.E., C.B., C.M.G., M.D., F.R.C.P.; Third Edition; 1936. London: The Actinic Press Limited. Demy 8vo, pp. 165, with illustrations. Price: 10s. 6d. net.

THE WOMAN ASKS THE DOCTOR, by E. Novak, M.D., D.Sc., illustrated by C. Clarke; 1936. London: Christophers. Demy 8vo, pp. 203, with illustrations. Price: 5s. net.

ORTHOPÆDIC SURGERY, by W. Mercer, M.B., Ch.B., F.R.C.S., F.R.S., with a foreword by J. Fraser, M.D., Ch.M., F.R.C.S.E.; Second Edition; 1936. London: Edward Arnold and Company. Royal 8vo, pp. 917, with illustrations. Price: 40s. net.

THE DIABETIC ABC: A PRACTICAL BOOK FOR PATIENTS AND NURSES, by R. D. Lawrence, M.A., M.D., F.R.C.P.; Fourth Edition; 1936. London: H. K. Lewis and Company Limited. Demy 8vo, pp. 70. Price: 3s. 6d. net.

PATHOLOGY OF THE NERVOUS SYSTEM: A STUDENT'S INTRODUCTION, by J. H. Biggart, M.D., with foreword by A. M. Drennan, M.D., F.R.C.P.; 1936. Edinburgh: E. and S. Livingstone. Demy 8vo, pp. 351, with illustrations. Price: 15s. net.

THE MEDICAL DICTATOR AND OTHER BIOGRAPHICAL STUDIES, by Major Greenwood, F.R.S., D.Sc., F.R.C.P.; 1936. London: Williams and Norgate Limited. Demy 8vo, pp. 213. Price: 7s. 6d. net.

## Diary for the Month.

AUG. 11.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
AUG. 11.—Tasmanian Branch, B.M.A.: Branch.
AUG. 14.—Queensland Branch, B.M.A.: Council.
AUG. 18.—New South Wales Branch, B.M.A.: Ethics Committee.
AUG. 18.—Tasmanian Branch, B.M.A.: Council.
AUG. 19.—Western Australian Branch, B.M.A.: Branch.
AUG. 20.—New South Wales Branch, B.M.A.: Clinical meeting.
AUG. 24.—Federal Council.
AUG. 25.—New South Wales Branch, B.M.A.: Medical Politics Committee.
AUG. 26.—Victorian Branch, B.M.A.: Council.
AUG. 27.—South Australian Branch, B.M.A.: Branch.
AUG. 27.—New South Wales Branch, B.M.A.: Branch.
AUG. 28.—Queensland Branch, B.M.A.: Council.
SEPT. 1.—Tasmanian Branch, B.M.A.: Council.
SEPT. 2.—Western Australian Branch, B.M.A.: Council.
SEPT. 2.—Victorian Branch, B.M.A.: Branch.
SEPT. 3.—South Australian Branch, B.M.A.: Council.
SEPT. 4.—Queensland Branch, B.M.A.: Branch.
SEPT. 7.—New South Wales Branch, B.M.A.: Organization and Science Committee.
SEPT 8.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

## Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser", pages xviii, xix. and xx.

CUNDERDIN DISTRICT HOSPITAL, CUNDERDIN, WESTERN AUSTRALIA: Medical Officer.

PUBLIC SERVICE BOARD, SYDNEY, NEW SOUTH WALES: Resident Medical Officer.

ROYAL HOSPITAL FOR WOMEN, PADDINGTON, NEW SOUTH WALES: Junior Resident Medical Officer.

SYDNEY HOSPITAL, SYDNEY, NEW SOUTH WALES: Honorary Assistant Anæsthetist.

THE WOMEN'S HOSPITAL, CROWN STREET, SYDNEY, NEW SOUTH WALES: Resident Medical Officers, Honorary Officers.

## Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment referred to in the following table without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

| BRANCHES. | APPOINTMENTS. |
|---|---|
| NEW SOUTH WALES: Honorary Secretary, 135, Macquarie Street, Sydney. | Australian Natives' Association.<br>Ashfield and District United Friendly Societies' Dispensary.<br>Balmain United Friendly Societies' Dispensary.<br>Friendly Society Lodges at Casino.<br>Leichhardt and Petersham United Friendly Societies' Dispensary.<br>Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney.<br>North Sydney Friendly Societies' Dispensary Limited.<br>People's Prudential Assurance Company Limited.<br>Phœnix Mutual Provident Society. |
| VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne. | All Institutes or Medical Dispensaries.<br>Australian Prudential Association, Proprietary, Limited.<br>Mutual National Provident Club.<br>National Provident Association.<br>Hospital or other appointments outside Victoria. |
| QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane. | Brisbane Associate Friendly Societies' Medical Institute.<br>Proserpine District Hospital.<br>Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY Hospital are advised, in their own interests, to submit a copy of their Agreement to the Council before signing. |
| SOUTH AUSTRALIAN: Secretary, 207, North Terrace, Adelaide. | All Lodge appointments in South Australia.<br>All Contract Practice Appointments in South Australia. |
| WESTERN AUSTRALIAN: Honorary Secretary, 205, Saint George's Terrace, Perth. | All Contract Practice Appointments in Western Australia. |
| NEW ZEALAND (Wellington Division): Honorary Secretary, Wellington. | Friendly Society Lodges, Wellington, New Zealand. |

## Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such a notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rates are £1 for Australia and £2 5s. abroad *per annum* payable in advance.